

Pro Bono Bio

Survey conducted into patient experience of life with osteoarthritis. A collaboration between Pro Bono Bio, Arthritis Research UK, and LloydsPharmacy

Executive summary

Over 400 people with joint conditions completed an on-line survey between January and May 2014. Of these, 268 had a doctor's diagnosis of osteoarthritis (OA) with the remaining respondents citing other conditions such as rheumatoid arthritis, gout or pain post injury. The purpose of the survey was to better understand the impact of this condition on patients' lives and to determine the 'real-life' use of currently available treatments and the potential interest in new treatments, such as the drug-free gel – FLEXISEQ®. According to a recent report by Arthritis Research UK,¹ OA affects nearly nine million people in the UK and costs the NHS £5.2bn in direct healthcare costs. However, several studies assessing the burden of OA in the EU demonstrated that, in active patients, the indirect costs (such as loss of productivity of patients themselves or their caregivers) were actually greater than the direct costs thus illustrating the economic impact on society of this condition.² Because of the symptoms experienced by patients and the fact that many of them also have other medical conditions, the management of their condition is a real challenge for the patients themselves and their healthcare teams.

Three out of four patients with OA have problems with mobility despite taking one or more treatments

Of those surveyed, 97% reported some restriction of movement, and over 70% of patients reported that they have a very noticeable reduction in movement or can hardly move due to their joint condition. Not surprisingly, this results in them struggling with or being unable to carry out daily activities such as walking, climbing stairs, etc., and participating in sporting activities. In an attempt to improve their symptoms, the vast majority of respondents with OA (90%) were taking drug-based medicines with a significant 75% of patients taking more than one treatment to try and manage their condition. This clearly demonstrates that patients struggle to reduce the pain and stiffness of their joints and continue to add in new treatments.

Some patients are using too many oral NSAID pain killers

Many patients (57%) take a pain pill from the class of medication known as non-steroidal anti-inflammatory drugs or NSAIDs. This class of medicine includes aspirin, ibuprofen, naproxen, celecoxib and diclofenac; some are prescribed by doctors while others can be bought from a pharmacy over the counter (OTC). However, this class of medicine is well known to cause side

effects, especially in patients who have risk factors. These risk factors include being elderly (usually defined as over 65 years), having conditions such as high blood pressure, having ulcers, having had a previous heart attack or stroke, or taking certain other medications. Extremely worrying is the significant number of patients (19%) who report that they are taking two oral NSAIDs at the same time. Although we do not have dose information, it seems likely that these patients will be taking at least one NSAID pill at the maximum recommended dose and then taking a second to achieve further relief. This means that they could be exceeding recommendations for the total amount and number of NSAIDs taken – either because of the combined dose taken or because of taking more than one concurrently. Taking two NSAIDs will have no additive benefit over simply increasing the dose of an individual NSAID but does have an increased risk of side effects such as gastric bleeds, heart attack or stroke.

A quarter of patients with OA were using a topical NSAID alongside an oral NSAID

Likewise, use of topical and oral NSAIDs concurrently is of concern as it increases the patient's overall exposure to NSAIDs, is unlikely to give greater symptom relief and is something that should only be done with caution and after discussion with a doctor.

Over half of the patients taking oral NSAIDs should only do so with caution and additional monitoring

This survey found that just under two-thirds (58%) of the patients taking an oral NSAID had another condition which meant they should either be closely monitored or should avoid taking these pills all together. These patients should be encouraged to seek medical advice to ensure that appropriate treatment is in place.

Nearly half of the patients report to have had side effects due to their OA treatments

Just under half of the patients (48%) reported having already experienced side effects due to their medication taken for OA and/or the pain and symptoms associated with their OA so it is not surprising that 86% said they had some concerns over the side effects their medications may be causing. However, worryingly, more than one-third could not list any side effects known to be associated with their medications and hence were not aware of the potential risks of their treatments.

New effective and safe treatments are needed

To understand what patients are looking for in new treatments, they were presented with a list of product features and asked to rank these in order of importance. Given the impact of pain and loss of joint function on their lives, it was not surprising that reduction of these were top of the ranking, followed by being drug-free and having no side effects.

A new topical treatment for the pain and stiffness of OA has recently been launched – FLEXISEQ®. As it is a completely novel approach, it was of interest to understand – in a blinded fashion – how interested patients would be in this product. When presented with a blinded product profile of a new drug-free topical treatment which has been shown to have comparable efficacy to the oral NSAIDs¹⁶ but with vastly better safety and tolerability, respondents were particularly interested in the fact that it was drug-free, and over 99% expressed interest or said they would like to try it.

Conclusion

The survey results illustrate that doctors and patients struggle to control the pain and joint stiffness caused by OA with a vast majority of patients reporting a major impact on mobility and daily activities^{1,3,4}. The reliance on NSAIDs by these patients is of great concern due to the well-known issues with these drugs; especially in those patients with certain other medical conditions which puts them at a higher risk of the side effects. The patients taking more than one oral NSAID – thereby probably exceeding recommendations – are at an even greater risk of these side effects. This reinforces the need for good communication between doctors and patients to make sure that prescribing doctors are aware of all the treatments that patients are using. It is therefore not surprising that there was great interest in a new drug-free treatment which has proven pain and stiffness relief, but none of the issues of the oral NSAIDs.

Background

Osteoarthritis (OA) is a very common condition that results in painful and stiff joints, can impact mobility and have a major effect on patients' quality of life.^{3,4} It is a condition that usually affects older people, but there are a significant number of younger sufferers, often as a result of injury or strain put on joints by repetitive exercise. The incidence of OA is growing, due to the ageing population, and also rising rates of obesity.⁵

There is no cure for OA and many of the available treatments for the symptoms of the disease do not work for all patients⁶ or are unsuitable for use by many patients.⁷⁻¹¹ In particular, there has been much attention given recently to the concerns and issues with non-steroidal anti-inflammatory drugs (NSAIDs). These tablets are widely taken by patients, both on prescription from their doctors and bought over the counter (OTC), and many patients do gain some pain relief from them. However, it is well known in the medical profession that many patients should not be taking NSAIDs on a regular basis due to their increased risk of side effects or the risk of the NSAIDs interfering with other medications. These include patients with high blood pressure, patients taking blood thinning agents such as warfarin, or those with a history of gastric problems who do not take a protective co-medication.⁷⁻¹¹ In addition, elderly patients with OA, already at a higher risk of complications from NSAID use,¹² often have other medical conditions (co-morbidities) and risk factors for NSAID-related side effects. One study reports that 29% of patients with OA also have hypertension and 18% have dyspepsia.¹³

We conducted a survey to explore how patients with OA perceive their condition and to determine the 'real-life' use of treatments and interventions. It is important to know how well patients understand the advice and information given to them, and therefore whether the real use of medication reflects the best clinical guidance.

A further objective of the survey was to find out what patients with OA are particularly looking for in new treatments and how well these attributes – presented in a blinded fashion – match those of a new treatment for the pain and stiffness of OA, namely FLEXISEQ®. FLEXISEQ® was launched in the UK at the end of 2013 and has been the subject of increasing media interest. This drug-free treatment has been shown to provide comparable pain relief to an oral NSAID and has an excellent safety and tolerability profile.¹⁴⁻¹⁷ It has a novel approach to treating the symptoms of OA and can be used by all patients and be purchased without prescription. Such advances are very rare and we were interested in understanding patient interest in this treatment.

Survey methods

Respondents with joint pain were recruited to take part in the on-line survey via the Arthritis Research UK website and among teams in LloydsPharmacy stores between January and May 2014. The patients completed a background survey, including questions regarding their joint pain, diagnosis, symptoms, previous treatments, current treatments and knowledge of any side effects of treatment.

To address the objective of understanding interest in a new treatment, the respondents on the Arthritis Research UK website then went on to complete the section about desired attributes in new

treatments and their interest in trying a new product which was presented as an anonymous product profile (but based on the attributes of FLEXISEQ®). The LloydsPharmacy teams did not complete this section as they have previously been informed specifically about FLEXISEQ®, would recognise the profile and would skew the results.

Results

Most patients in the survey had OA

Overall, 440 patients were recruited to the survey across the UK, including 137 LloydsPharmacy colleagues and 303 patients via the Arthritis Research UK website. The majority of patients were female (388 patients; 88%). In about two-thirds (61%), the patient's joint pain had been diagnosed by their doctor as OA (Table 1).

Table 1. Doctor's diagnosis of the joint pain condition*

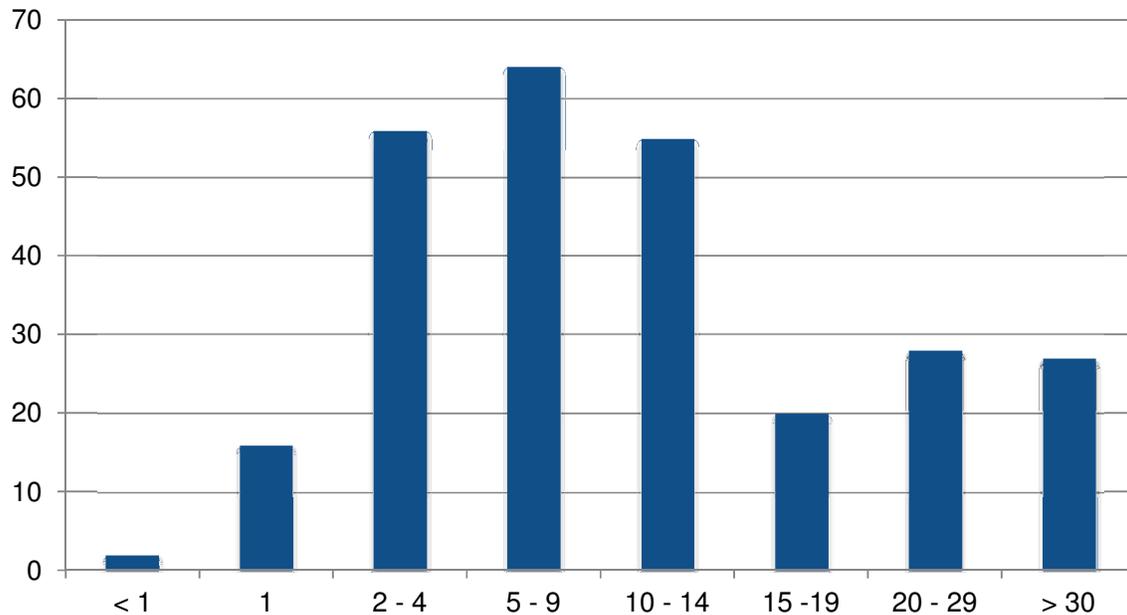
| Diagnosis of joint pain | Number of patients* | % of patients* |
|-------------------------|---------------------|----------------|
| Osteoarthritis | 268 | 61 |
| Rheumatoid arthritis | 121 | 28 |
| Other | 92 | 21 |
| Strain/sprain | 29 | 7 |
| Bursitis | 25 | 6 |
| Gout | 14 | 3 |

*More than one diagnosis could be made in each patient

Background details of the patients with OA

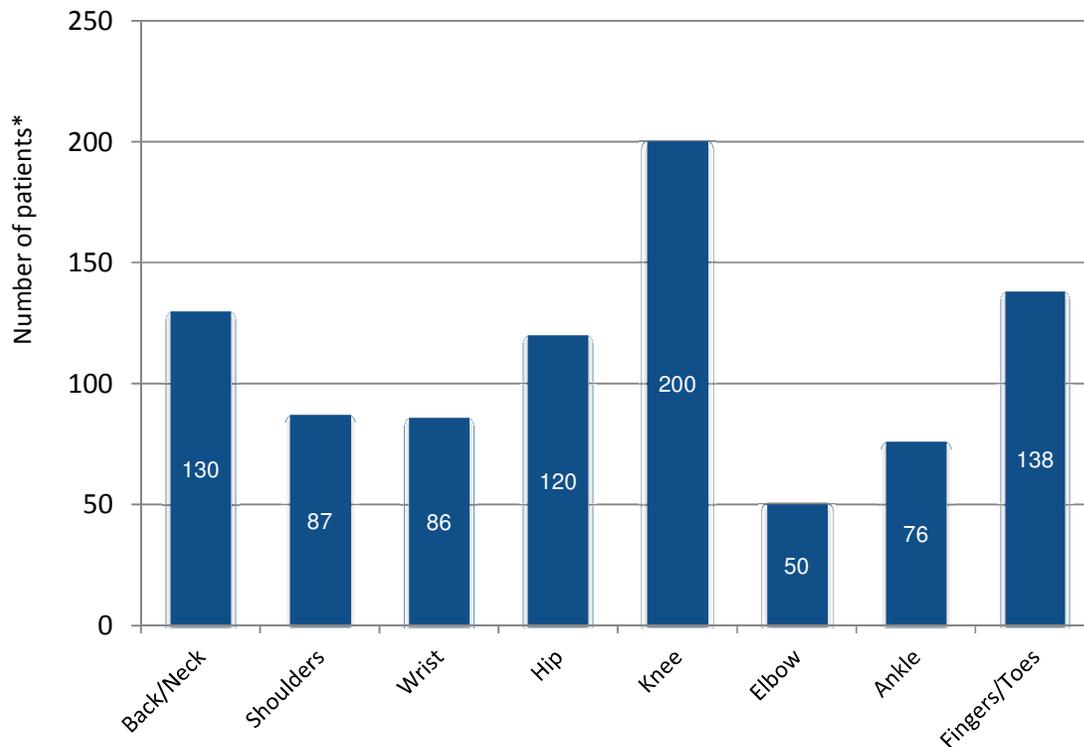
Within the group of patients with OA (268 patients; 61% of all patients in the survey), patients were aged between 23 and 91 years, with most between 50 and 60 years (95 patients; 35%) or 60 and 70 years (74 patients; 28%). Patients had been living with OA for an average of 11.11 years (Figure 1).

Figure 1. Patients with OA: years of having had OA



Consistent with the OA population, the joint most often affected by OA was the knee (Figure 2) and many patients had more than one affected joint.

Figure 2. Patients with OA: affected joint*

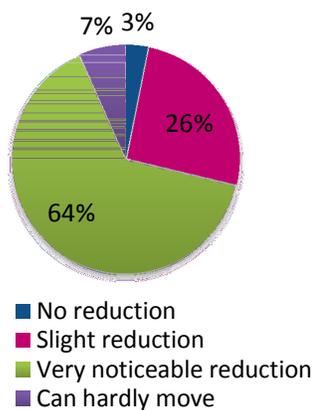


*Patients may have more than one affected joint

OA has a real impact on joint mobility

Despite using extensive medication (see later), 97% of patients reported some restriction of movement with 7% reporting they could ‘hardly move’ (Figure 3). This, of course, had led to the loss of a number of daily activities, such as walking (70% of patients), bending (28%), using their hands to open jars or write (27%) and also participation in sporting activities (40%).

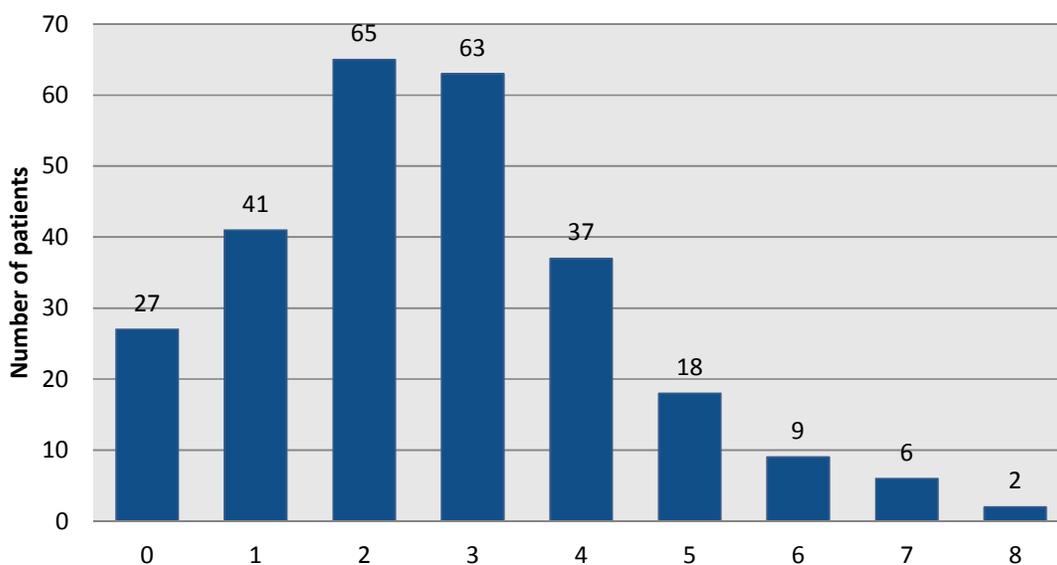
Figure 3. Impact of OA on movement



Ninety percent of patients with OA were taking at least one medication to manage their OA

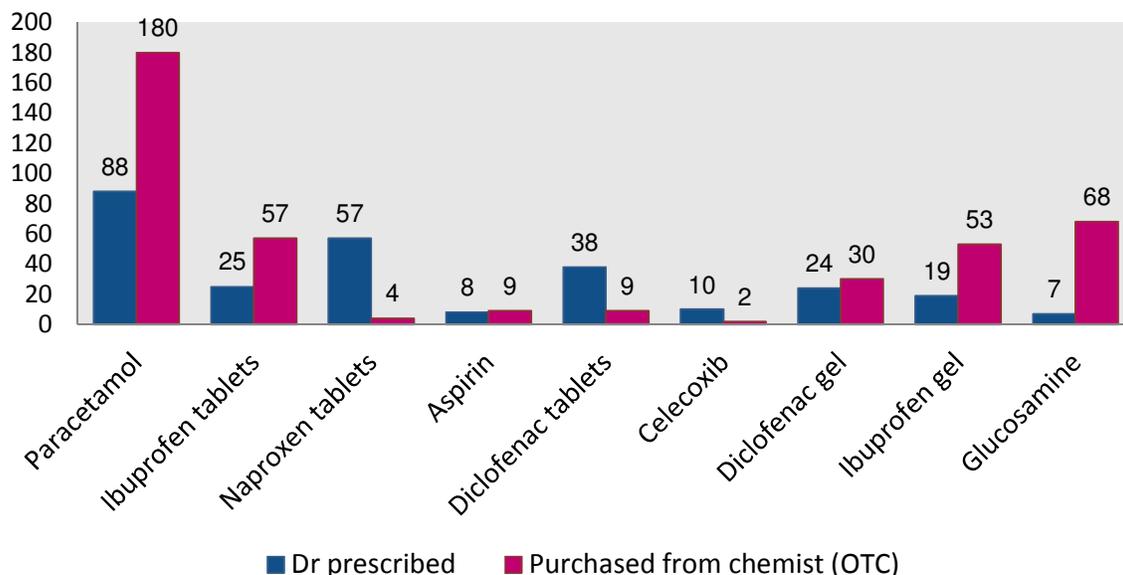
Of the patients with OA, 241 (90%) were using at least one drug-based treatment for their OA, either prescribed by their doctor, or purchased from the chemist (OTC) (Figure 4). 75% (200 patients) were taking more than one medication. The majority of these patients were using two (65 patients; 24%) or three (63 patients; 24%) different kinds of medication but some were taking up to eight different medications for their OA (Figure 4).

Figure 4. Current medications for OA



Paracetamol was the treatment used by most patients followed by ibuprofen tablets, glucosamine and ibuprofen gel. Eight patients (3%) were using pain relief not specified in the survey and 27 patients (10%) were not using any kind of OA medication or intervention (Figure 5).

Figure 5. Current medications for OA



For patients taking more than one treatment for their symptoms of OA, the most common combination was paracetamol plus a drug from the NSAID class (79%). Paracetamol was most frequently used in combination with ibuprofen tablets (32% of patients) or glucosamine (21%). Although aspirin would not normally be considered a treatment for the symptoms of OA, it was included in this section and in the ‘treatment for other conditions’ section as many patients understood that they were taking aspirin because it helped with their OA symptoms.

Some patients with OA were using more than one NSAID

In total, 152 of the 268 patients (57%) with OA were taking an oral NSAID (diclofenac, naproxen, ibuprofen, aspirin or celecoxib), with 52 of the patients with OA (19%) taking more than one oral NSAID at this time. Oral ibuprofen purchased OTC was the most commonly used NSAID as part of a dual oral NSAID regimen. Patients were most likely to be combining OTC oral ibuprofen with a different oral NSAID prescribed by their doctor.

In the 39 patients taking two concurrent oral NSAIDs, six patients had purchased both of these OTC, 14 patients had purchased one OTC and had the other one prescribed, and 19 patients stated that they had been prescribed both NSAIDs.

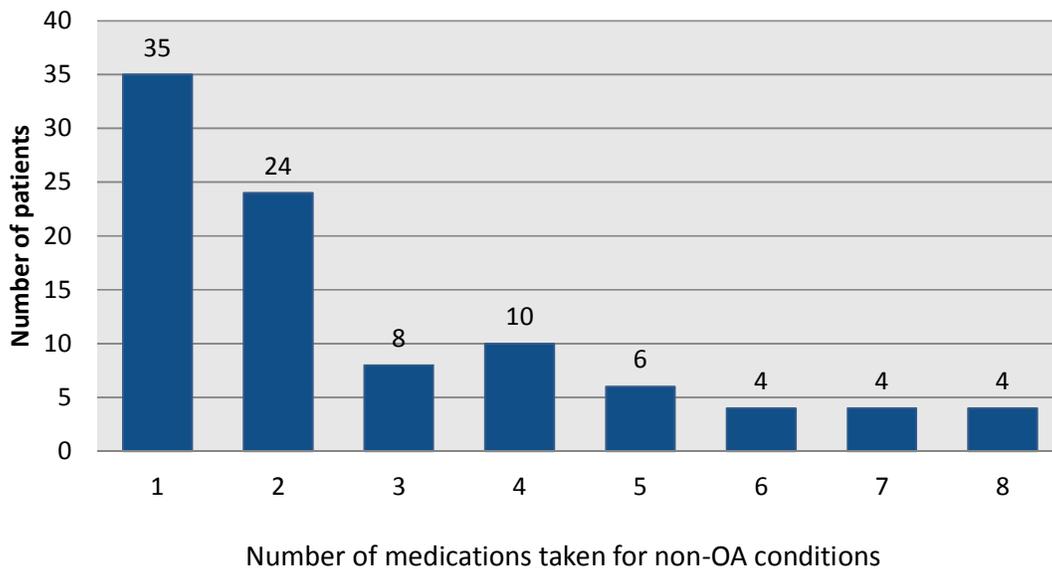
26% of the patients with OA were using a topical NSAID alongside an oral NSAID, with the topical NSAIDs both bought OTC and prescribed by the doctor.

Many patients with OA also had other medical conditions

More than half of the patients with OA (58%) had other medical conditions or co-morbidities, with 55 patients (21%) having two or more co-morbidities.

Within the group of patients taking oral NSAIDs, 87 patients (57%) had other medical conditions which are known to have issues with these pills. The most common co-morbidities were hypertension (47 patients), hyperlipidaemia (30 patients) and asthma (25 patients). Of these patients, 63% were taking at least one other medication for these co-morbidities as well as for their OA. Some patients were taking up to eight different medications plus any medication for their OA (Figure 6).

Figure 6. Number of medications taken for non-OA conditions

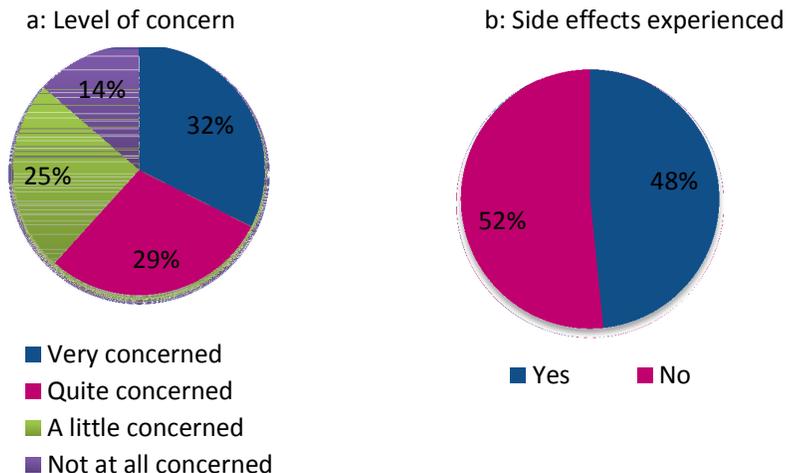


At least 20% of the patients taking oral NSAIDs either had a condition causing concern and/or were taking another medication with a specific warning for use alongside the oral NSAID.

Nearly 50% of patients with OA have experienced side effects attributed to their OA medication

Of patients responding to the question, 48% had experienced a side effect they believed to be due to their OA medication. Of the patients who were taking at least one medication, 35% were not aware of side effects associated with their OA medication but 86% of patients did have concern over potential side effects (Figure 7). In patients who were aware of side effects, there was reasonable correlation between what they stated and the listed side effects for the medications they were using.

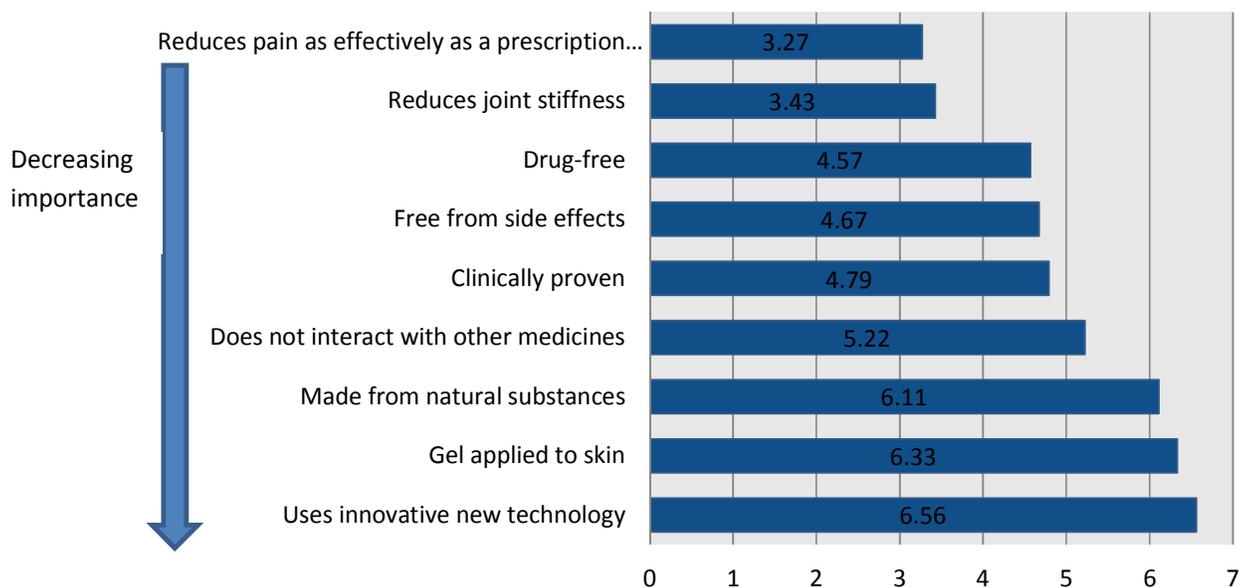
Figure 7. Level of concern over side effects (a) and side effects experienced due to OA medication (b)



Effects against symptoms of OA were the most important features for a new product

Respondents ranked features of a new product according to interest (1 = most important, 9 = least important), and reduction in pain and reduction in joint stiffness were ranked as the most important (mean 3.27), with being drug-free and having no side effects next (4.57 and 4.67) (Figure 8).

Figure 8. Ranking of importance of features for a new treatment for OA



When presented with a product profile of a new drug-free topical treatment which has been shown to have comparable efficacy to the oral NSAIDs but with vastly better safety and tolerability (FLEXISEQ®), respondents were particularly interested in the fact that it was drug-free and over 99% expressed interest or said they would like to try it.

Points for discussion

Many patients with OA continue to be troubled by their symptoms, despite the best efforts of their doctors and pharmacists, and in spite of using a number of drugs and interventions. Indeed, this survey showed that patients often turn to a combination of medicines, both prescribed and bought OTC, oral and creams/gels in an attempt to relieve their suffering. No one medication appears to provide sufficient and maintained pain relief, and many patients try multiple combinations in the hope of experiencing relief from their symptoms.

The use of multiple drugs at the same time can be hazardous. Paracetamol and oral NSAIDs were the most widely combined treatments for OA in this survey, in itself not a problem combination provided that the correct dosage recommendations are followed for both products. However, the NSAIDs have well-known safety issues, as reinforced last year with regards to the dangers of taking diclofenac.¹⁸ In addition, oral NSAIDs all have a warning that states they should not be used or can only be used with caution in patients with certain medical conditions or taking certain medicines. Of concern, therefore, is the 57% of patients in this survey, who are taking oral NSAIDs but also have other medical conditions putting them at greater risk of the side effects from their NSAIDs. These patients should be closely monitored and should seek medical advice to ensure that they are using their medications appropriately. These results clearly reflect medical publications, which show that many patients are using inappropriate medication combinations or taking medications that are not suitable for them.¹⁹⁻²¹

Of particular concern is the 19% of patients who reported taking more than one oral NSAID concurrently. Patients may not realise that ibuprofen, aspirin, diclofenac and naproxen are all in the same drug class (i.e. all NSAIDs), all have the same mechanism of action and that more than one should not be taken at a time. While combinations of different NSAIDs are unlikely to provide any greater pain relief than just taking a higher dose of one, the issue is the total dose taken. Although we do not have dose information in this survey, it would seem likely that patients would be taking the maximum dose of one of the NSAIDs and then adding the second due to unresolved symptoms. This means that they could be exceeding recommendations for the total NSAID dose. This will increase the risk of side effects. Indeed, patients are advised to take the lowest dose of the most appropriate NSAID for the shortest period of time to achieve pain relief which is incompatible with a chronic condition such as OA. Patients should be aware of these risks and should discuss their medication with a healthcare professional. In addition to the patients taking more than one oral NSAID, the 26% of patients using topical NSAIDs alongside an oral NSAID is also of concern. This increases the patients' total exposure to NSAIDs and the patient leaflets advise caution or consultation with a doctor before using these two formulations concurrently. The reasons for patients taking more than one were not explored, but could include:

- Misunderstanding GP directions to switch from one to another resulting in two being taken concurrently
- Lack of understanding that some of the pills bought at the pharmacy or supermarket, such as ibuprofen, are also NSAIDs
- The misconception that OTC medication is 'safe'.
- The belief that combining two painkillers is possible, based on the common advice to take paracetamol and ibuprofen at the same time

Although speculative, these types of concerns reinforce the need for clear patient communication and education (a point made in recent NICE guidelines). Patients must be aware of the need to tell their prescribing doctor of everything that they are taking/using and must have directions for use clearly explained to them.

Just under half of the patients (48%) reported having already experienced side effects due to their OA medication so it is not surprising that 86% said they had some concerns over the side effects their medications may be causing. However, a worrying 35% could not list any side effects known to be associated with their medications. This may be as a result of lack of information or a lack of understanding or both.

The reliance on multiple medications and the fact that many patients still suffer from symptoms highlight the need for alternatives with a totally different way of working. To explore what patients want from new treatments, they were presented with a list of product features and it is not surprising therefore, that relief from the pain and stiffness of OA were the features ranked most highly by patients. Being 'drug-free' was the third most important feature showing that despite a lack of patient awareness of side effects in a significant minority, safety was a recognised and important concern.

Virtually all patients (over 99%) were interested in or wished to try a new treatment which was presented to them anonymously showing the level of need. The product profile illustrated a new drug-free topical treatment which has been shown to have comparable efficacy to the oral NSAIDs but with vastly better safety and tolerability (FLEXISEQ®). Use of this product instead of oral and topical NSAIDs would avoid many of the side effects worrying the patients and would also cut down on the need for monitoring of patients on combinations of treatments that are putting them at risk.

Conclusion

This survey reflects medical publications which report that doctors and patients struggle to control the pain and joint stiffness caused by OA with a vast majority of patients reporting a major impact on mobility and daily activities. The reliance on NSAIDs by these patients is of great concern due to the well-known issues with these drugs, especially in those patients with certain other common medical conditions which put them at a higher risk of the side effects. There have been many medical publications recently focusing on the risk of these treatments for both healthy subjects and patients. The patients taking more than one oral NSAID – thereby possibly 'overdosing' – are at an even higher risk of these side effects. It is therefore not surprising that there was real interest in a new drug-free treatment – FLEXISEQ® – which has proven pain and stiffness relief, but none of the issues of the oral NSAIDs.

Acknowledgements

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