

A SURVEY OF THE USE OF GASTRO-PROTECTIVE AGENTS WITH NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN SURGICAL PATIENTS

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- **OBJECTIVE** - To survey the use of gastro-protective agents (GPAs) in patients receiving non-steroidal anti-inflammatory drugs (NSAIDs) for pain relief following surgery, and to develop and implement a prescribing policy.
- **DESIGN** - Patients receiving NSAIDs were surveyed, with gastro-protective agents and risk factors for NSAID therapy recorded. These results were compared with a retrospectively designed prescribing policy.
- **SUBJECTS AND SETTING** - Fifty patients on surgical wards were randomly selected for inclusion over a four-month period.
- **RESULTS** - Four patients (8 per cent) received a GPA without a valid indication. Seven patients (14 per cent) who did not receive a GPA were found to be eligible for such treatment. Eight patients (16 per cent) received the wrong dose of GPA, or the wrong choice of GPA. In addition, 10 patients (20 per cent) should not have received an NSAID because they had a history of gastro-intestinal problems.
- **CONCLUSION** - Nineteen patients (38 per cent) were not receiving appropriate GPA therapy according to a retrospectively implemented policy based on NICE guidance.

Surgical patients at Southampton General Hospital (SGH) generally receive the non-steroidal anti-inflammatory drug (NSAID) diclofenac post-operatively, unless contra-indicated, as part of their pain-management regimen. Diclofenac inhibits both cyclo-oxygenase (COX)-1 and COX-2, and is therefore considered to be a non-specific inhibitor of COX. Inhibition of COX-1 is associated with gastric ulceration due to the inhibition of the gastro-protective prostaglandins.¹ Inhibition of COX-2 is associated with the anti-inflammatory properties of NSAIDs.

Surgical patients require NSAIDs short-term. Short-term use, however, does not avoid the risk of developing complications. A review paper showed that those using NSAIDs short-term were at as much risk of gastric side effects as long-term users.² As a result, some patients who are receiving diclofenac also receive a gastro-protective agent (GPA) such as a proton pump inhibitor to prevent gastric side effects.

There was a perception by pharmacists that because there were no in-house guidelines, there was a variation in prescribing practice of GPAs with diclofenac within the surgery directorate, and pharmacists were intervening to rationalise therapy. A survey was set up, using principles from the National Institute for Clinical Excellence (NICE), to look at current prescribing of GPAs and NSAIDs and to develop guidelines if needed.³

The COX-2 selective inhibitors retain their anti-inflammatory action but have fewer incidences of gastric side effects because the COX-2 enzyme is not involved in the synthesis of gastro-protective prostaglandins.⁴ COX-2 selective inhibitors have recently been licensed for acute pain and could be considered for surgical patients with no cardiac problems instead of a standard NSAID and gastro-protective agent (GPA). COX-2 agents are not used routinely in patients with cardiac problems because of a possible link with an increased risk of myocardial infarction.⁵ A

study recently reported that patients receiving a proton pump inhibitor in conjunction with an NSAID were at the same risk of developing gastric side effects as those treated with a COX-2 agent alone.⁶ However, COX-2 selective agents were not investigated because they were not available on the formulary at the time of this study.

METHOD

A data collection form was designed to record risk factors for an adverse gastric event, dose and choice of GPA and surgical procedure in patients receiving an NSAID.

A pilot survey was conducted using this form to verify that all information required was being captured. Information was obtained from the patient drug chart, medical notes, nursing Kardex and from the patient by interview. Ten patients were involved in the pilot, which highlighted some flaws in the survey form.

The modified form was then used to capture data on a further 50 patients who were prescribed diclofenac. These 50 patients were randomly chosen from the surgical wards over a period of four months. The pre-registration trainee visited wards whenever a project day was allocated on the pre-registration trainee rota.

NICE guidance was used to prepare a list of risk factors for NSAID therapy with the help of some of the consultants. The categorisation of risk factors is listed in Table 1 (p458). The full policy with individual risk factors listed is presented in Panel 1 (p458).

The results collected were compared to the proposed prescribing guidelines, which at this stage had not been implemented in the directorate.

RESULTS

Twenty (40 per cent) patients were prescribed a GPA with an NSAID. Four of these had been admitted on the therapy (these patients were excluded from the results). Therefore 16 patients were seen who

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Table 1: Risk factors for NSAID therapy

Category	
No risk	No risk factors
Low	Age is only risk factor
Moderate	1 risk factor (excluding age) or age and 1 other risk factor. No history of a gastrointestinal (GI) ulcer
High	Previous history of GI ulcer or 2 risk factors (excluding age)

were initiated on a GPA in hospital to cover side effects from diclofenac. A variety of GPAs and doses were used. When compared to the draft guidelines, yet to be introduced at the time of the study, only four patients were found to have appropriate prescriptions. Twelve patients were inappropriately co-prescribed GPAs. Four patients did not have any risk factors and so did not need any GPA, and the remaining eight patients were prescribed an agent or a dose which was inappropriate.

Thirty patients (60 per cent) were seen who were prescribed diclofenac without a GPA. They were assessed for risk factors. Of these, 17 patients were identified as high/moderate risk, 10 had a history of GI problems and should not have received a NSAID. The remaining seven patients had moderate risk factors and should have received a co-prescription for a GPA. The remaining 13 patients had low or no risk factors and were treated appropriately with no GPA. The results are summarised in Table 2 (p459).

COST IMPLICATIONS

The cost of inappropriate GPA prescribing for two weeks' treatment was calculated to be £100.52. With the total cost of GPA prescribing as per the guidelines for two weeks of £94.64, a cost saving of £5.88 was identified. The cost calculations exclude patients initiated on a GPA in primary care.

The inappropriate GPA prescribing figure is the cost of the GPA therapy for the 12 patients who were started on these agents in hospital for prophylaxis with diclofenac, but who did not have any risk factors or were prescribed an agent or dose not advocated by the new guidelines. Under the new guidelines the 12 patients would either not have received any GPA or a different dose or agent would have been prescribed.

Panel 1: Pre- and post-operative surgical patients

Guidance on prescribing of gastro-protective agents with short term diclofenac

Before initiating a patient on any NSAID, the patient should be assessed for risk factors for gastro-intestinal (GI) side effects using the table below. Based on these risk factors, a gastro-protective agent should be prescribed as indicated by the patient's risk factors. NSAIDs should be used with caution in patients with asthma, renal disease or any history of indigestion.

NSAIDs should always be prescribed in conjunction with regular paracetamol and as required/regular dihydrocodeine if tolerated.

All prescriptions for prophylactic agents must state "for prophylaxis with diclofenac".

Risk factors:-

- Patients aged 65 years or over
- Those already taking other medicines that are known to increase the likelihood of GI complications, eg, steroids, warfarin
- Those on selective serotonin re-uptake inhibitor antidepressants (fluoxetine, paroxetine, citalopram, sertraline, fluvoxamine)
- Those with serious co-morbidities, eg, liver disease or renal disease
- Those requiring the prolonged use (more than 8 weeks) of maximum recommended doses of standard NSAIDs
- Those with a history of GI problems (eg, history of dyspepsia or previous symptoms with NSAIDs but no significant gastroscopically detectable GI lesions)

Choice of gastro-protective agent

Patients undergoing moderate/major GI surgery

	Gastro-protective agent
Nil by mouth	Ranitidine 50mg <i>tds</i> IV
Tolerating orals	Lansoprazole 15mg <i>om</i>

All other surgical patients who receive regular NSAIDs

	Gastro-protective agent
No risk factor	Nil
Low risk	Nil
Moderate risk	Lansoprazole 15mg <i>om</i>
High risk	Use alternative analgesic

For long term treatment, refer to trust guidelines

The appropriate GPA prescribing figure is the cost of lansoprazole 15mg daily for all of those patients identified as "at risk" during the survey. It excludes the 10 patients who were classified as high risk who may have required alternative analgesia.

DISCUSSION

The results of the survey showed that 29 patients (58 per cent) did not receive appropriate prescriptions for NSAIDs or

GPAs. This highlights the need for education and guidelines on assessment of patient risk factors and prescribing these drugs.

The major area of concern was the 17 patients (34 per cent) who did not receive any GI prophylaxis but were at high risk of developing GI toxicity. Of these 17 patients, 10 should not have received diclofenac because they had a history of GI problems. If alternative analgesia did not provide relief, they may have been appropriate for a

Table 2: Results of survey

Drugs prescribed	n	Appropriate	Inappropriate	Excluded
NSAID + GPA	20	4	12	4*
NSAID with no GPA	30	13	17	0

* Four patients were admitted on an NSAID, and were excluded from the results

trial of a COX-2 inhibitor. COX-2 agents were not on the hospital formulary, but were available for specific patients on the request of a consultant. The remaining seven moderate-risk patients should have been prescribed a GPA.

Age is identified by NICE as being a risk factor for NSAID therapy. However, elderly patients are more sensitive to the side effects of medicines, may be confused about their treatment and be taking multiple drugs. Therefore this factor has not been used alone to start a GPA in a surgical patient. Elderly patients should be assessed individually, monitored closely and NSAID therapy stopped immediately if there are any symptoms of indigestion.

A large proportion of patients included in the study receiving co-prescriptions for GPAs were prescribed these inappropriately. Of these 12 patients, four patients had no risk factors and did not require a co-prescription and the remaining eight patients either received doses of GPA which were larger than the recommended prophylactic dose or an agent which was thought to be insufficient based on their risk factors. Inappropriate prescribing has financial implications for the National Health Service (NHS) in terms of drug costs and potential gastrointestinal toxicity, which could lead to admission to hospital and therefore additional cost. These problems could be minimised if patients were

carefully assessed for the identified risk factors and given the correct treatment from the beginning.

The main problem encountered in developing guidelines was the lack of evidence to prove the benefit of using a GPA with diclofenac post-operatively to prevent ulceration. Published evidence relates to long-term therapy in medical patients, but not in surgical patients. The guidelines at SGH indicate the use of lansoprazole 15mg as the prophylactic agent of choice. This is based on licensed indications, published evidence and cost. Another difficulty encountered was in grading the risk factors. Evidence in this area is limited and so has been omitted from these guidelines at this stage.

The results of this survey led to the agreement of the proposed GPA/diclofenac prescribing guidance by the consultants in directorate, and the trust's drugs committee. This guidance was therefore implemented within the directorate.

Many assumptions were made when conducting a cost analysis of this audit data. However the final figure did show that the introduction of these new guidelines would be cost neutral. This was a useful result as there was a perception by the pharmacists that the introduction of these guidelines

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would result in additional expenditure. It was not possible to include potential expenditure for alternative analgesia in patients unsuitable for any NSAID under the new guidelines. Alternative agents may or may not be more expensive.

This project focused on assessment of risk factors for GI side effects. It identified an area where work was needed to improve patient care and standardise therapy. This project has not addressed the issue of indications for use of COX-2 selective agents (even if this were cheaper than using an NSAID in conjunction with lansoprazole 15mg) because at the time of writing COX-2 selective inhibitors were not available on the hospital formulary. However a consultant could still authorise these agents for an individual patient if needed.

The survey needs to be repeated to ensure compliance with the guidelines. When this survey is repeated it may be appropriate to include COX-2 agents, and this is clearly an area for further work.

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Ethics committee approval

This survey was registered with the clinical effectiveness department at the Southampton University Hospitals NHS Trust, which was normal practice for a project of this type.

It has, in the past, been the understanding that only invasive research on patients had to go before an NHS ethics committee. The Central Office for Research Ethics Committee states that this is no longer the case. Research on NHS patients, ie, those subjects recruited by virtue of their past or present treatment by the NHS (including those treated under contract with the private sector) are still included in the list of types of research that require ethical approval. Research that involves access to records of past and present NHS patients or the use of, or potential access to, NHS premises or facilities (including NHS staff), must also be reviewed independently by a local research ethics committee to ensure that it meets ethical standards.

Undergraduate projects, preregistration projects, postgraduate degree projects, PhD research and service evaluations all fall within the scope of this advice.⁷

It is therefore recognised that work of this nature should now be reviewed independently by a local research ethics committee.

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