Prescribing patterns and administration of intravenous paracetamol: a clinical audit

Abstract

Background: Intravenous (IV) paracetamol was authorised by the Irish Medicines Board in 2003. Thereafter, the Drugs and Therapeutics Committee (DTC) in the study hospital added the IV preparation to the hospital formulary in September 2005. The DTC policy allows for IV administration only when the oral (PO), rectal (PR) and enteral routes are not available.

Aim: To identify the prescribing and administration patterns of IV paracetamol, to assess its appropriateness and to identify the associated opportunity cost.

Methods: A retrospective survey was conducted on patients who were prescribed paracetamol on adult medical and surgical wards. The patients were randomly selected and their healthcare charts were reviewed over a two-week period in September 2008.

Results: A total of 1,934 administrations were surveyed. Compliance with policy was demonstrated in 94.3% of administrations. The opportunity cost of using IV instead of PO tablets was found to be in excess of €23,000 per annum for the study hospital.

Conclusion: The majority of paracetamol administration was compliant with hospital policy. The cost implications for inappropriate administration were identified by calculating the difference incurred when IV was chosen over the equally efficacious PO/PR routes. Current findings and recommendations can be presented to relevant stakeholders (doctors, nurses and pharmacists) in order to review the usage of IV paracetamol and improve adherence with policy guidelines.

Key words: Intravenous paracetamol, clinical audit, audit cycle, prescribing guidelines.

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Introduction

In 2003, Intravenous (IV) paracetamol (Perfalgan®) was authorised for the Irish market by the Irish Medicines Board (IMB). It is indicated for the short-term treatment of moderate and severe pain following surgery and for the treatment of fever.[1] Oral (PO) or rectal (PR) administration of paracetamol is as effective as IV administration, and should therefore be used as first-line routes of administration.[1] The bioavailability of paracetamol varies depending on the route of administration. IV paracetamol provides onset of pain relief within five to 10 minutes after administration.[1] PO preparations are completely absorbed from the gastrointestinal tract with a peak plasma concentration in 30 to 60 minutes. The bioavailability of suppositories is approximately 80% of that of tablets.[1] Clinical trials to date have concentrated on the morphine-sparing effects of IV paracetamol and have indicated that although morphine consumption was reduced, pain control was no greater.[2]

The Drugs and Therapeutics Committee (DTC) in the study hospital added the IV preparation to the hospital formulary in September 2005. The DTC policy states that IV paracetamol may only be prescribed by the acute pain team, intensive care team or by anaesthetists, and is justified only when the PO and PR routes are unavailable.[3]

The availability of PO administration can be determined by whether the patient is pre-operative and 'nil per mouth'. Factors such as dysphagia and vomiting are additional considerations. The PR route is unavailable if the patient is non-mobile (e.g., post-operative) or has gastro-intestinal symptoms (e.g., diarrhoea).

The IV route of administration is associated with a higher incidence of anaphylactic reactions.[2] Also, the therapeutic value of the parenteral route is not supported by a thorough comparative evaluation.[4]

There is a significant cost difference between the IV and either the PO or PR preparations of paracetamol available in the Irish market. These differences highlight the potential saving in choosing a cheaper but equally efficacious oral tablet over the IV route, which is over 200 times the cost.[5] The acquisition cost associated with a 1g dose of an oral tablet is four cents; for an oral soluble tablet is 55 cents; for a suppository is €2.30; and, for an IV solution is €8.28. In addition, the IV solution requires the use of IV administration sets and constitutes an invasive procedure.

The aim of this paper is to identify the prescribing and administration patterns of IV paracetamol, to evaluate adherence to hospital policy standards, to identify reasons for non-adherence and to identify the associated opportunity costs.

Methods

The study design was a clinical audit conducted as a retrospective cohort survey. Clinical pharmacists were asked to identify patients on the general medical and surgical wards who were prescribed IV paracetamol during a two-week period (September 15-26, 2008). Patient identification numbers were randomised and 198 patients were selected. Data were collected on 108 patients (80%) for whom records were successfully retrieved from the Medical Records Department; the remainder of the records were not available.

The data collection form was designed to collect information on patient demographics (gender, age, length of hospital stay, clinical indication for paracetamol, bowel status, fluid status, mobility status) and procedural details (surgical procedure undertaken, date, time and type of procedure).

Information was also collected on each dose of paracetamol administered to the patient, the route of administration and the availability of the PO or PR routes at the time of each administration.

Data were collected retrospectively by reviewing healthcare records, and adherence to policy for each administration was ascertained by the availability of the PO or PR routes when IV paracetamol was administered. Targeted parameters included patient mobility, and bowel and fluid status. Details of whether the patient was 'nil per mouth' were noted, along with medicines administered by a non-IV route.

Data were entered into SPSS v. 15 and descriptive and inferential statistics are reported. The opportunity cost for paracetamol was calculated per annum and quantifies the monetary difference incurred when IV was chosen over the PO/PR routes.

Results

Some 51.9% of the study population analysed was male, the median age was 59 years (range 16-91) and the majority (81.5%) received surgical care. Greater than one-third (37%) of patients were under the care of general surgery, followed by orthopaedics (26%), medical (19%), and vascular surgery (7%), and the remainder were a mixture of gynaecology, urology and ear, nose or throat (10%). The majority (69.4%) underwent a minor or major procedure during their stay as an inpatient.

A total of 1,934 administrations were surveyed for the 108 patients. The most common prescription (87.2%) included IV plus another route. The other routes available were PO or PR and the choice of route rested with the nurse administering the medication. The route administered in the majority was PO (91.1%), IV (7.4%), PR (0.7%), or via enteral feeding tube (0.8%). The factors associated with selection of route are described below.

Adherence with prescribing policy

Review by the acute pain team was documented in the healthcare record for 18.5% of patients, and a recommendation to use IV paracetamol was documented in the healthcare record for one patient (0.9%). The prescriber was not discernible in the majority of cases and so it could not be determined if the prescription was generated by intensivists or anaesthetists. The prescription was co-signed by the pharmacist in 85% of cases, and in 47.2% of cases they added a qualifying comment to the drug prescription and administration chart (the Kardex) to advise use of PO or PR routes as first-line therapy. In eight patients, the choice of IV/PO/PR paracetamol was prescribed but not administered.

Adherence with administration policy

Adherence with hospital DTC administration policy was demonstrated in 94.3% of administrations. Of the IV doses administered, the OR route was available in 53.8% and the PR route was available in 92.7% of the cases.

Exploring reasons for non-adherence

There was a statistically significant association between the ward in which the patient received care and adherence to policy, indicating that adherence was more likely on some wards than others ($\chi 2=19.38$, df=9, $p=0.022$). Also, there was an association between the prescription type and adherence, i.e., doses

Table 1: Association between prescription type (regular, once off, or as required) and compliance with DTC administration policy ($\chi 2=8.746$, $p<0.05$).

Prescription type	Compliance (%)		
	Yes	No	n
Regular	95.1	4.9	1,534
Once off	100	0	7
As required	91.3	8.7	393
n	109	1,825	1,934

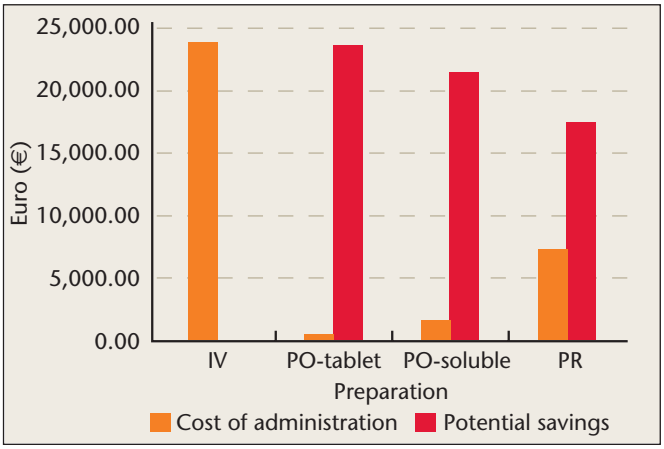

FIGURE 1: Cost of IV paracetamol per annum against PO and PR formulations. Unit cost per 1g of paracetamol: IV (€8.28); PO-tablet (€0.04); PO-soluble (€0.55); and, PR (€2.30).[5]

prescribed 'as required' were less compliant than those for regular or once-off administration ($\chi 2=8.746$, df=2, p=0.013) **(Table 1)**. There was no association between adherence and doses administered day time (07:00-21:00) or night time (21:00-07:00) ($\chi 2=0.238$, df=1, p=0.328). There was a weak association between adherence and endorsement of the qualifying comment on the Kardex by the clinical pharmacist, although this was not statistically significant ($\chi 2=0.238$, df=1, p=0.09).

Of those patients who underwent a procedure, there was an association between non-adherence and the time from procedure to administration. The results indicate that non-adherence was greatest on the day of procedure after the PO route became available ($\chi 2=141.6$, df=5, $p<0.001$) **(Table 2)**. There was no association between the specialty team overseeing patient care and adherence ($\chi 2=1.608$, df=4, p=0.807) ($\chi 2=0.792$, df=1, p=0.272), or between patient gender and adherence ($\chi 2=0.298$, df=1, p=0.397).

Calculating costs

During the two-week study period, a total of 1,934 administrations of paracetamol were recorded, which extrapolates to 50,284 administrations annually. Considering that 5.7% of the total 1,934 administrations were administered as IV when other routes were available, this would result in 2,866 non-adherent administrations per annum. The cost difference incurred by choosing the more expensive IV formulation over the cheaper but equally efficacious and safe PO formulation was found to be €23,615.84 per annum for the study hospital **(Figure 1)**.

Discussion

The high level of adherence (94.3%) to policy is encouraging because of its implication for patient safety and cost effectiveness. However, there is a 200-fold difference between the ingredient cost of an IV versus a PO dose of paracetamol.[5] This difference may vary depending on the market but it generally holds that IV solutions are considerably more expensive. For example, in Australian hospitals, Ghiculescu *et al* found that IV formulation is 100-fold the cost of PO and two-fold the cost of PR.[6] Advantages of IV are accuracy of dose delivered to the patient and targeted peak analgesic effect **(Figure 1)**.[7] To date, there has been no published data to justify the cost of IV over other routes.[8] It should be expected, therefore, that restrictions on IV use form part of hospital policy.[6,7,8]

Indentifying conditions associated with non-adherence may provide an opportunity for implementing effective change. For example, wards that were shown to have lower compliance can be targeted for education and training. The finding that non-adherence was greatest on the day of a procedure may reflect a misperception that IV administration is more potent than other routes or a reluctance to use the PR route, either on the part of the patient or staff member. This is important to consider as the vast majority of patients audited received surgical care. IV paracetamol was most often administered post-operatively, even after the patient food intake restrictions were lifted **(Table 2)**. The duration of IV use was not noted in the medical chart, nor was a recommendation to review the method of administration. This may have resulted in the administration of IV beyond when other routes may have become suitable.

Despite the prescribing restrictions, it is possible that junior medical staff may have prescribed the drug. This was unclear because the prescriber did not include their training level beside the prescription, and therefore it cannot be ascertained if the acute pain team, anaesthetist, or other medical staff on call made the recommendation.

Clinical pharmacists aim to maximise the appropriate use of IV paracetamol by labelling the drug Kardex with "Use PO or PR first line, as effective as IV". It is unclear whether or not this influences compliance and it may be worthwhile to consider alternative strategies, such as implementing an automatic stop on IV paracetamol beyond 48 hours unless reviewed by the pain team or anaesthetist. Another consideration could be to empower the clinical pharmacist to amend the Kardex, as appropriate, on their review.

Table 2: Association of the duration between procedure and administration with compliance to DTC administration policy ($\chi 2$=141.6, p<0.05).

Time of IV paracetamol administration with respect to procedure	Compliance (%)		
	Yes	No	n
Day before	99.1	0.9	228
Day of	72.6	27.4	106
Day after	87.2	12.8	179
Two days after	93.8	6.3	160
Three days after	97.9	2.1	143
Four+ days after	97.9	2.1	625
n	1361	80	1441

Non-compliance with "as required" prescriptions might be overcome by discontinuing the choice of the IV route once PO/PR routes become available. Ideally, PO should replace IV once the patient is able to eat solids and swallow oral drugs.

Lamb *et al* highlighted the problem of idiosyncratic ordering and administration of paracetamol. They concluded that hospital guidelines for paracetamol should be more specific in terms of indication for use and to ensure that the medical staff is precise in what their prescription of paracetamol means.[9] IV paracetamol is a relatively new preparation and there is limited safety data available to date, and so its use should strictly follow formulary guidelines.[9] Most published studies have concentrated on whether its use results in a reduction in morphine consumption and little has been published comparing IV to PO or PR for either pain control or the treatment of fever.[10] Clinical trials to date have had small sample sizes and this may contribute to the lack of statistical significance of their results.[4] We recognise the limitations of this study, but for the future we recommend that this type of audit be performed in a greater number of patients and in additional hospitals and medical centres.

Conclusion

We recommend that prescribing IV paracetamol should be restricted to the pain, intensive care and anaesthetic teams. It should be prescribed only for short-term treatment and reviewed after 48 hours by the authorised prescribers. This audit found that the majority of IV paracetamol administered in general medical and surgical adult patients was compliant with DTC policy. Non-adherence was associated with specific wards, prescription type and the duration between procedure and administration. The annual cost of administering IV over PO preparations was in excess of €23,000.

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