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Original research

Outpatient management of biliary colic: A prospective observational study of prescribing habits and analgesia effectiveness☆

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ABSTRACT

Background: Uncomplicated biliary colic presents a significant health and financial burden to hospitals and primary care services alike. There is little guidance on the correct analgesia to use on an outpatient basis. This study aimed to evaluate the effectiveness of oral analgesics on biliary colic pain and to explore the prescribing habits of community doctors.

Methods: Consecutive patients with ultrasound proven symptomatic gallstones completed a questionnaire recording demographics and symptomatology. Pain was assessed using a visual analogue scale (VAS) based on the Biliary Symptom Score (BSS) to evaluate the effectiveness of various analgesic agents. Local General Practitioners were also surveyed to establish prescribing practices.

Results: Co-Codamol had the highest mean effectiveness VAS score (6.5/10). Patients with increased BMI, short symptom duration and a BSS >70 were most likely to suffer from severe pain. Patients in a subgroup with severe pain were most likely to have their pain reduced by NSAID analgesia compared to no NSAID (OR 2.20, $p = 0.027$). This effect remained significant upon multivariable regression (OR 2.52, $p = 0.018$) in a model containing age and NSAIDs. There was wide variation in the prescribing practice of GPs and hospital doctors.

Conclusions: The range of drugs prescribed for biliary colic is extensive with little evidence base. In this study NSAIDs were the most effective analgesia for patients with severe pain. In the absence of contraindications to their use, physician education or guidance emphasizing the benefits of NSAIDs may potentially reduce symptomatic hospital presentation and admissions for biliary colic.

1. Introduction

Biliary colic (BC) is the term used for gallbladder (GB) pain experienced by patients without overt infection around the gallbladder. The pain is located in the epigastrium or right upper quadrant of the abdomen and is typically colicky in nature due to muscular spasm of the GB wall secondary to outflow tract obstruction.[1] BC affects 1–4% of the adult population known to suffer with cholelithiasis (gallstones) and is the most common presenting symptom.[2]

In the United Kingdom (UK) episodes of BC are usually managed with oral analgesia at home and settle spontaneously. However, referral or self-presentation to hospital is often required if there is diagnostic uncertainty or severe pain uncontrolled by available analgesia. When a patient presents with biliary colic the most important immediate step is adequate symptom control including appropriate analgesia. There is good evidence for administration of NSAID analgesia for patients presenting to the Emergency Department with acute biliary colic.[2,3] It is less clear what analgesia these patients should be prescribed for outpatient management of their pain.

Where patient preference and general health permit surgery, the gold standard treatment for biliary colic and gallstones is laparoscopic cholecystectomy (LC). In the UK the timing of LC varies according to patient choice, waiting list length and local hospital policy. Current practice is divided between centres providing 'hot' gallbladder services involving LC during the index admission and those who schedule an elective interval LC. Both clinical and economic aspects of these approaches have been examined previously

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and remain under consideration.[4–7] Currently, there is a lack of clear guidelines recommending one option over the other. Thus many patients are discharged to manage symptomatic disease in the community while awaiting interval surgery or in preference to surgery. This results in a significant number of subsequent hospital admissions for patients with recurrent biliary colic, unable to control their pain with oral analgesia. These admissions present an additional healthcare burden; in the National Health Service (NHS) there were 105,910 hospital admissions for cholelithiasis in 2010–2011.[8]

There is a paucity of guidance in the published literature regarding the relative efficacy of analgesic regimes patients receive on discharge with the existing literature largely relating to inpatient or emergency department treatment.[9,10] Consequently, patients who present to their community General Practitioner (GP) rather than a hospital are given analgesia according to anecdotal factors such as personal preference or previous experience rather than evidence based practice.

This study investigated the relative patient-reported effectiveness of different analgesia regimes for outpatient management of BC and compared these to current community physician (General Practitioner) and hospital doctor prescribing practice.

2. Methods

2.1. Patients and setting

University Hospital of Coventry & Warwickshire is a large teaching hospital and tertiary referral centre offering a full range of general surgery services. Over an 8-month period, consecutive patients booked for laparoscopic cholecystectomy were included in the study and filled out a questionnaire during their pre-operative clinic appointment. Each patient had the presence of gallstones confirmed by ultrasonography. This study was undertaken as part of an audit of service in the general surgery unit. Clinical audit approval was granted by the hospital's Quality & Effectiveness Department.

2.2. Patient questionnaire

The authors formulated a questionnaire based on the information required to calculate the Biliary Symptom Score (BSS).[11] Several iterations of this were trialed prior to a final version. Repeated practice meetings were held to ensure a consistent approach to data collection by the researchers. The questionnaire recorded information regarding both prescribed and over the counter medications and did not discriminate between them. Patients were asked to rate, on a visual analogue scale (VAS),[12] the severity of their pain with 0 rating as 'no pain' and 10 as 'severe pain'. VAS were also used to assess the subjective effect of the analgesic at reducing pain with 0 rating as 'no effect' and 10 as 'no pain'.[13] The questionnaire was non-mandatory and completion was taken as consent to participate. The questionnaire can be seen in Appendix 1.

In addition to the patient questionnaire general practitioners (GPs) from the local area were surveyed. All participants were asked to return an answer to each of the questions outlined below on a private digital keypad during an HPB surgery teaching session:

1. "Your patient has gallstones, what do you prescribe for future biliary colic attacks?"
2. "The patient returns asking for stronger analgesia, now what do you prescribe?"

The options given to the GPs were "Nothing, Buscopan, Codeine, NSAID, Pethidine tablets, Oramorph, Something else or Don't know." Answers were returned using digital keypads ensuring privacy.

2.3. Inclusion and exclusion criteria

Patients included were adults with a diagnosis of biliary colic undergoing elective laparoscopic cholecystectomy following ultrasound confirmation of gallstones within their gallbladder. Patients were excluded from the study if they were unable to remember the dosages of analgesia they were taking and this information could not be retrieved from the electronic discharge summary. Any medication that could not be administered orally was excluded from the study.

2.4. Data analysis

A previously reported Biliary Symptom Score[11] was calculated for patients based on their questionnaire responses. Patient characteristics were compared using the Chi-squared test. Patients were divided into subgroups according to the severity of their pain on presentation (a VAS score of >7 was considered to be severe pain). A significant reduction in pain was defined as a reduction of $\geq 50\%$ of the post-analgesia VAS compared to the presenting VAS.

Univariate and multivariate logistic binary regression models were built to determine predictors of significant pain reduction. An odds ratio (OR) and corresponding 95% confidence interval (CI) which were greater than 1.0 indicate an increased association of the predictor variable (e.g. analgesic use) with the outcome (significant pain reduction), indicating a useful outcome. Variables which carried a significance of $p < 0.1$ at univariable level were entered into a multivariable model, and were selected using a forward stepwise process and if their p-value remained <0.05.

Data were collected and entered into Microsoft Excel 2011 (Microsoft Corporation, Redmond, USA) for descriptive analysis. Data were analysed using SPSS 18.0 (SPSS Inc, Chicago, Illinois). Financial conversions from £GBP to $USD and €Euro are based on prevailing market rates on 22nd July 2013 using the UK Forex exchange rate, rounded to the nearest whole unit of currency.

3. Results

3.1. Demographics

A total of 210 consecutive patients were asked to complete the questionnaire, 7 patients were unable to remember the name or dose of analgesia they were taking and were therefore excluded leaving 203 patients in the study. Of these 155 (76%) were female and 48 (24%) were male. Almost half ($n = 97$ patients, [48%]) of the patients were >50-years-old with 71 (35%) being 30–50-years-old and 35 (17%) being 18–30-years-old (see Table 1). Ethnicity of patients was recorded with 171 (84%) classifying themselves as white

Table 1
A summary of basic patient demographics.

	Male	Female	Total
n total	48 (24%)	155 (76%)	203
n 18–30 years	2 (6%)	33 (94%)	35 (17%)
n 31–50 years	14 (20%)	57 (80%)	71 (35%)
n 50 + years	31 (32%)	66 (68%)	97 (48%)
Mean BMI	28.16	28.96	28.56
On pre-existing analgesia	9 (28%)	23 (72%)	32 (16%)

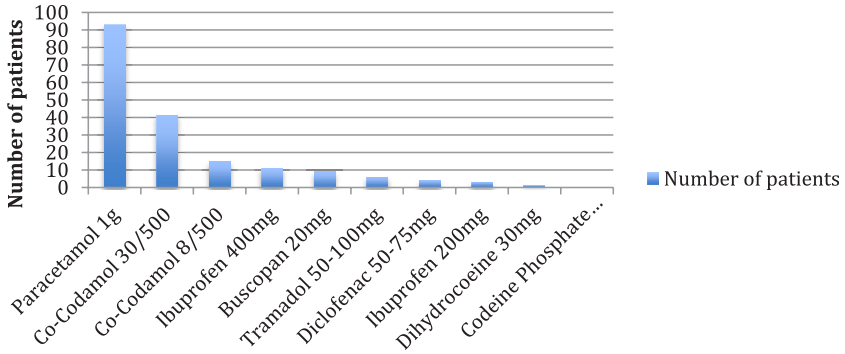

Fig. 1. A bar chart showing the 1st choice of analgesic agent for monotherapy patients.

British, 22 patients (11%) as Asian and 10 (5%) as Afro-Caribbean. The mean BMI was 28.8 (18.5–46.9).

3.2. Analgesic choice

93 patients (46%) were supplied with Paracetamol for first-line pain relief with a further 25 patients using it as a second-line analgesic. The second most commonly used agent was Co-Codamol 30/500, which was used first-line in 41 (20%) patients and second-line in 12 patients. NSAID analgesia was used first-line in only 10% of patients. Buscopan was commonly used as a third-line therapy (see Fig. 1). The preferred mode of analgesia was monotherapy with 181 patients (89%) opting for this over combination therapies.

3.3. Perceptions of pain by different groups

Overall, 147 patients (72%) had experienced BC symptoms for longer than six-months. Patients under 30-years of age subjectively reported the most severe pain with an average VAS of 9/10. Those patients aged 30–50 experienced less severe pain (8.6/10). Patients over 50 years of age experienced the least severe pain with a mean score of 8.3/10; there were no significant differences between these groups in terms of pain VAS scoring. Female patients rated their pain as more severe than male patients with a mean VAS score of 8.6/10 compared to 8.1/10. The majority who were taking regular analgesia for a pre-existing co-morbidity had lower limb osteoarthritis (34 patients [17%]).

3.4. Comparison of reported-effectiveness

Co-Codamol tablets (30 mg/500 mg) had the highest post-analgesia mean VAS score of 6.5/10 followed by tramadol. Both NSAIDs (Diclofenac and Ibuprofen) had lower mean VAS scores than opiate medications with Paracetamol having the lowest score of 3.85/10 (see Fig. 2). There were no significant differences between the post-analgesia mean VAS scoring for different agents.

There were 166 patients with severe pain (a VAS score >7). These patients were most likely to have an increased BMI, a shorter duration of symptoms and a Biliary Symptom Score >70 (see Table 2). Those with a VAS score >7 were most likely to be taking either NSAID or opioid analgesia in their analgesia regime, not necessarily as a 1st choice (see Table 2). Patients with severe pain were most likely to have their pain reduced by 50% or more when treated with NSAID analgesia compared to no NSAID (OR 2.20, $p = 0.027$). This effect remained significant upon multivariable regression (OR 2.52, $p = 0.018$) in a model containing age and NSAIDs (see Table 3). The effect seen with opioid medications was not significant (OR 0.87, $p = 0.680$).

4. General practitioner prescribing practice

A total of 124 local GPs participated in the survey. There was no clear pattern or agreement between GPs when asked about their initial prescription for a BC patient. A quarter opted for Buscopan (26%), Codeine (23%) or an NSAID (25%). The other quarter of participants opted for stronger analgesia with 14% choosing Pethidine tablets and 8% choosing Oramorph. There were 10 abstentions (a response rate of 92%).

If the patient returned for stronger analgesia 23% of GPs stated they would prescribe Oramorph, 17% an NSAID, 15% Pethidine, 14% Codeine and 11% Buscopan. However, 18% of GPs stated they would choose something else entirely or that they wouldn't know what to prescribe and 32 GPs abstained (a response rate of 74%), indicating a substantial degree of variation in their practice. These results are available in Table 4 and Fig. 3.

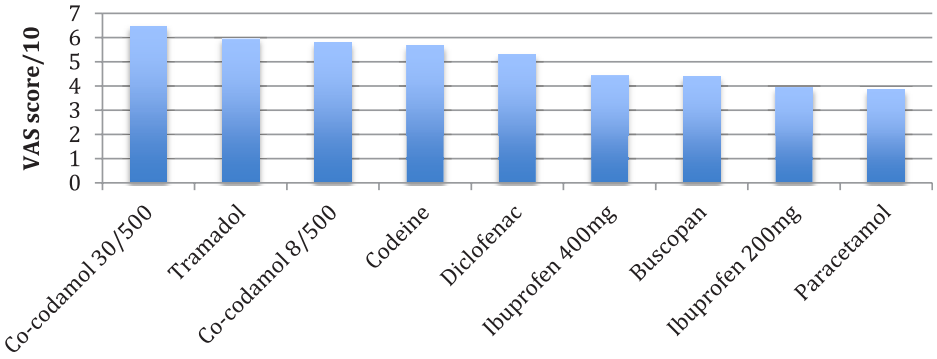

Fig. 2. A bar chart showing the mean post analgesia VAS scores.

Table 2
Analysis of factors associated with severe pain (represented by VAS > 7).

Factor	Sub-group	Total *n* (%)	VAS ≤ 7 *n* (%)	VAS > 7 *n* (%)	*p* Value
Age (years)	18–30	35 (17.2%)	3 (8.1%)	32 (19.3%)	
	31–50	71 (35.0%)	12 (32.4%)	59 (35.5%)	
	50+	97 (47.8%)	22 (59.5%)	75 (45.2%	0.168
Gender	Male	48 (23.6%)	12 (32.4%)	36 (21.7%)	
	Female	155 (76.4%)	25 (67.6%)	130 (78.3%)	0.164
Ethnicity	White British	167 (82.3%)	28 (75.7%)	139 (83.7%)	
	Asian	24 (11.8%)	7 (18.9%)	17 (10.2%)	
	Afro-Caribbean	12 (5.9%)	2 (5.4%)	10 (6%)	0.335
Body Mass Index	BMI ≤ 25	46 (22.7%)	13 (35.1%)	33 (19.9%)	
	BMI > 25	157 (77.3%)	24 (64.9%)	133 (80.1%)	0.045
Symptom duration (months)	1–3	24 (11.8%)	1 (2.7%)	23 (13.9%)	
	3–6	36 (17.7%)	4 (10.8%)	32 (19.3%)	
	>6	143 (70.4%)	32 (86.5%)	111 (66.9%)	0.048
Chronic illness	Not present	170 (83.7%)	30 (81.1%)	140 (84.3%)	
	Present	33 (16.3%)	7 (18.9%)	26 (15.7%)	0.627
Biliary symptom score	≤70	111 (54.7%)	26 (70.3%)	85 (51.2%)	
	>70	92 (45.3%)	11 (29.7%)	81 (48.8%)	0.035
Analgesia taken (Either NSAID or Opioid)	No NSAID	141 (69.5%)	20 (54.1%)	121 (72.9%)	
	Taking NSAID	62 (30.5%)	17 (45.9%)	45 (27.1%)	0.024
	No opioid	79 (38.9%)	24 (64.9%)	55 (33.1%)	
	Taking opioid	124 (61.1%)	13 (35.1%)	111 (66.9%)	<0.001

5. Discussion

The main finding of this study was that Co-Codamol is the most effective agent for biliary colic patients. Overall the analgesic agents prescribed for biliary colic have relatively poor effectiveness with a highest post-analgesia VAS of 6.48 for Co-Codamol tablets. The secondary finding of this study is that NSAID analgesia is the most effective agent for a subset of patients suffering from severe pain. These patients tended to be obese with a high biliary symptom score and a shorter duration of symptoms. In addition to this, it was identified that patients prefer analgesic monotherapy to combination therapy. There was no consensus in the GP group regarding appropriate prescribing for biliary colic, they tended to prescribe either an NSAID or weak opioid initially which is consistent with the patient questionnaire results. However, GPs advanced up the pain ladder more swiftly than their hospital colleagues by way of prescribing Oramorph or Pethidine for a greater number of their patients than hospital doctors. The broad spread of analgesic agents used for biliary colic by GPs and hospital doctors is likely due to a lack of evidence-based guidelines, leading to individualized prescribing habits and preventable variation in practice. In addition, the higher number of GP abstentions to the second question indicates a degree of uncertainty regarding the appropriate analgesia for refractory BC.

Table 4
Initial analgesia and stronger analgesia prescribing choices from community GPs.

Drug	Initial choice ($n = 124$)	Stronger choice ($n = 124$)
Nothing	1	2
Buscopan	24	11
Codeine	22	3
NSAID	24	4
Pethidine tablets	12	13
Oramorph	8	20
Something else	3	15
Don't know	20	24

Literature regarding analgesia in biliary colic is, for the most part, restricted to recommendations on treatment used in the emergency department[14] or administered parenterally.[15] Selected literature investigating the role of analgesia in acute biliary colic attacks performed during the last 25 years is displayed in Table 5. It is clear that the majority of studies recommend NSAIDs for treatment of acute biliary colic in the Emergency Department; the best analgesia for outpatient management remains unclear.

Additional significance of this study lies in the fact that BC presents a substantial financial burden to health services. It is estimated that uncomplicated BC admissions in English hospitals cost the NHS £23,829,750 (approximately $36,535,808 or €27,698,527) in 2010–2011 (assuming a 1-night inpatient stay).[8,16] Our study suggests that a streamlining of the approach to outpatient management of BC could help to reduce the number of hospital admissions, leading to an associated cost saving.

Despite easy availability, NSAIDs were used less commonly than we expected in this study. There are several possible reasons for this. Codeine and other weak opioids commonly cause constipation, an inconvenient side effect, but not life-threatening. NSAIDs, especially in the younger population are relatively safe but have some serious side effects including increased risk of gastrointestinal haemorrhage and acute kidney injury.[17–19] These factors may persuade patients to avoid NSAIDs. It may have also dissuaded doctors from prescribing NSAIDs more commonly, especially to those at risk of side effects such as elderly or asthmatic

Table 3
Univariate and multivariate regression for a ≥50% reduction in VAS score.

Factor	Sub-group	Univariable			Multivariable		
		Odds ratio	95% Confidence intervals	*p* Value	Odds ratio	95% Confidence intervals	*p* Value
Age (years)	18–30	Ref		0.047	Ref		0.035
	31–50	3.325	1.237–8.935	0.017	3.085	1.125–8.463	0.029
	50+	2.946	1.132–7.668	0.027	3.648	1.345–9.896	0.011
Gender	Male	Ref					
	Female	0.997	0.470–2.115	0.994			
Ethnicity	White British	Ref		0.390			
	Asian	1.033	0.363–2.936	0.952			
	Afro-Caribbean	0.332	0.068–1.622	0.173			
Body Mass Index	Value > 25	0.821	0.380–1.774	0.616			
Symptom duration (months)	1–3	Ref		0.180			
	3–6	0.363	0.118–1.111	0.076			
	>6	0.465	0.183–1.183	0.465			
Chronic Illness		1.993	0.842–4.718	0.117			
Any NSAID		2.202	1.094–4.432	0.027	2.517	1.171–5.410	0.018
Any opioid		0.868	0.442–1.704	0.680			

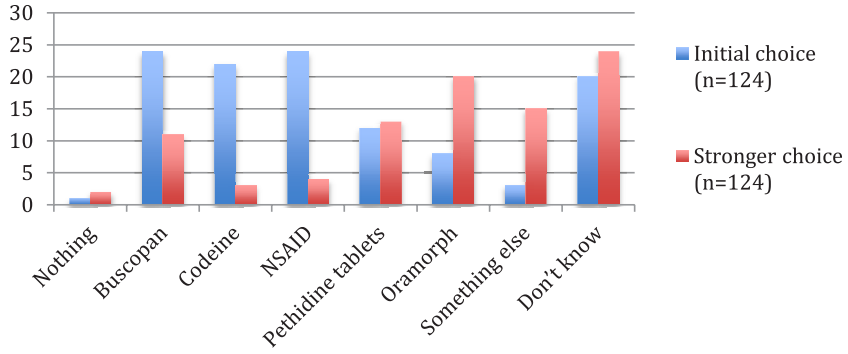

Fig. 3. A bar chart showing the initial and stronger analgesia choices of GPs.

Table 5
Summary of previous studies reporting comparative efficacy of analgesic agents in biliary colic.

Author	Year	Study design	Level of evidence	Setting	Conclusion
Basurto et al.[10]	2008	Systematic review & meta-analysis	1++	ED	NSAIDs are the analgesia of choice for uncomplicated biliary colic and prevent progression to cholecystitis
Kumar et al.[15]	2004	Randomized, blinded study	2+	ED	IM Diclofenac gives better pain relief than IM Hyoscine and prevents progression to cholecystitis
Colli et al.[9]	2012	Meta-analysis	1++	ED	NSAIDs are first choice treatment for biliary colic. Opioids have similar efficacy but more complications
Akriviadis et al.[22]	1997	RCT	1+	ED	IM Diclofenac is a more effective painkiller than IM Saline and reduces progression to cholecystitis
Goldman et al.[23]	1989	Randomized double-blinded study	2+	ED	Diclofenac is the analgesia of choice in acute biliary colic and may decrease progression to cholecystitis
Olsen et al.[2]	2008	Randomized double-blinded	2+	ED	Both Ketorolac and Butorphanol are reasonable choices for treating acute biliary colic
Henderson et al.[3]	2002	Randomized trial	2+	ED	Both Ketorolac and Meperidine are effective in treating acute biliary colic
Schmieder et al.[24]	1993	Randomized single-blinded	2+	ED	Metamizole is a more effective painkiller in acute biliary colic than Tramadol and Butylscopolamine

Level of evidence as per the SIGN grading system, developed by The Scottish Intercollegiate Guidelines Network.[25]
ED = Emergency Department; IM = Intra-muscular.

patients. In addition to this one of the differential diagnoses for biliary colic is gastritis/gastro-oesophageal reflux disease, a condition that can be exacerbated by NSAID use.

The severity of pain experienced by patients in this study is worst in young females and decreases with increasing age and male sex. There may be several contributing factors to this such as acceptance of pain in older age groups or those on pre-existing medications (there were 32 [16%] in this study). However other studies have found that gender and age cause no significant difference in significant VAS scores.[20] This underlines the point that a patient's genotype and phenotype may both have a role to play in both perception of and response to pain.

One of the strengths of this study is the large sample size of patients limiting the effects of participant bias. The broad sample of GPs also means that prescribing habits from a wide region were captured, eliminating the potential for localized habits to affect the survey results, which may make the findings more generalizable to other areas of the UK.

There are limitations of this study; one of these is the subjectivity of VAS. Given the inevitable heterogeneity of pain interpretation in patients some inconsistency in this respect was unavoidable. There will be a degree of participant recall bias resulting from patients being asked to recall the severity of their symptoms at an unspecified interval. This study only looks at those patients who are scheduled for operative intervention, therefore the extent to which these results can be extrapolated to patients treated conservatively is unknown. Although cases are defined on the basis of having been listed for surgery following ultrasound findings consistent with gallstone aetiology, these patients have not been followed through post-operatively so we cannot definitively say their symptomatology was secondary to gallstones. Rates of post-cholecystectomy syndrome vary in the literature between 10 and 15% so this phenomenon could potentially be a cofounding factor.[21]

Optimization of oral medication is important for biliary colic patients and further research in this area is needed before the most effective analgesia for outpatient management of biliary colic can be established. It is clear from the results of this study that doctors do not know what to prescribe their biliary colic patients. Future work should concentrate on validating objective metrics to measure analgesia effectiveness in the setting of biliary colic, such as morbidity and hospital admission rates.

6. Conclusions

This study has shown the degree of variance and uncertainty in outpatient prescribing for biliary colic. It remains important to individualize medication to ensure that the benefit of potentially harmful drugs such as NSAIDs outweigh the risks to the patient. A prospective randomized study exploring this issue is required before clear guidance can be given to doctors on outpatient prescribing for biliary colic.

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Ethical approval

Approved as a clinical audit by the Quality & Effectiveness department at UHCW Number 778.

Author contribution

Study design – All authors.
Data collection – Johnston, Greaves, Prew.
Data analysis – Johnston, Fitzgerald, Bhangu, Greaves.
Drafting of the manuscript – All authors.
Approval of the final manuscript – All authors.

Conflicts of interest

None declared.

Appendix 1

Outpatient analgesia for biliary colic questionnaire

Hospital number:	Body-mass index:
Age:	Ethnicity:
Gender:	

How long have you been experiencing pain from your gallstones (please specify weeks, months or years)?

Do you take painkillers for any other medical condition other than your gallstones?

If so, which painkillers do you take?

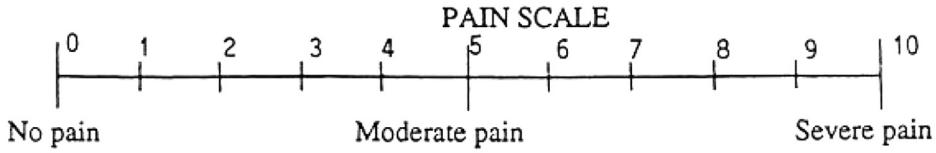
What dosage(s) do you take?

How often do you take this/these painkillers?

What other symptoms do you suffer from other than pain when you get an attack? (e.g. vomiting, yellow skin, diarrhoea)

Have you ever suffered from cholecystitis (a gallbladder infection), cholangitis (infection of the bile ducts) or pancreatitis (inflammation of the pancreas)?

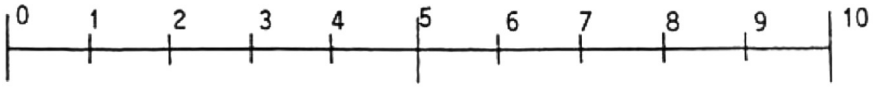
On the scale below please rate the severity of your gallstone pain before you take any painkillers:



What painkiller do you take first for your gallstone pain?

What dosage and how many tablets?

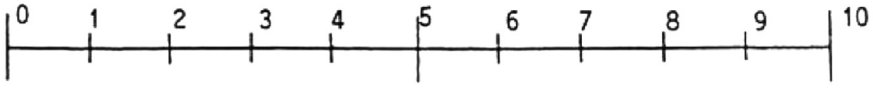
Please mark on the scale below how effective this painkiller is at relieving your pain (0 = **no effect** and 10 = **no pain**)



Do you take a 2nd painkiller? What is it called?

What dosage and how many tablets?

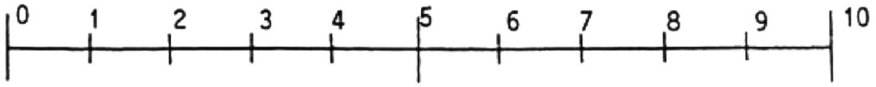
Please mark on the scale below how effective this painkiller is at relieving your pain (0 = **no effect** and 10 = **no pain**)



Do you take a 3rd painkiller? What is it called?

What dosage and how many tablets?

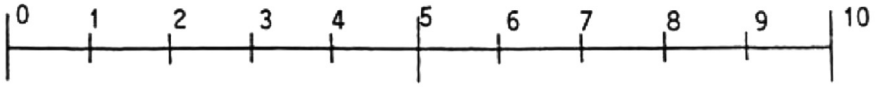
Please mark on the scale below how effective this painkiller is at relieving your pain (0 = **no effect** and 10 = **no pain**)



Do you take a 4th painkiller? What is it called?

What dosage and how many tablets?

Please mark on the scale below how effective this painkiller is at relieving your pain (0 = **no effect** and 10 = **no pain**)



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