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ABSTRACT

Objective This study analysed the analgesic effect and changes in vital signs associated with administration of inhaled Methoxyflurane (MTX) and/or intranasal Fentanyl (INF) for prehospital management of visceral pain.

Method A retrospective, observational study reviewing 1024 randomly selected records of patients with presumed visceral pain administered MTX (465), INF (397) or both (162) by the Western Australian Ambulance Service between January 2004 and February 2006. Clinical variables assessed included systolic blood pressure, pulse rate, respiration rate and Glasgow Coma Scale score. Pain was assessed utilising Visual/Verbal Analogue Scale pain scores.

Results Overall effects on vital signs appeared favourable 5 min after use and at hospital arrival with either agent alone or in combination. As sole agents, MTX produced the greatest initial pain scores reduction (2.0 (1.7 to 2.2) vs 1.6 (1.4 to 1.8)) (mean (95% CI), and INF provided greater pain reduction by hospital arrival (3.2 (2.9 to 3.5) vs 2.5 (2.1 to 2.9)). While both agents were effective, INF provided a greater pain score reduction for cardiac (3.0 (2.6 to 3.4) vs 2.3 (1.8 to 2.8)), female (3.4 (2.9 to 4.0) v 2.5 (2.0 to 3.0)) and age 75+ patients (3.2 (2.5 to 3.8) vs 1.8 (1.0 to 2.5)). Combined use of agents was not advantageous.

Conclusions MTX and INF are effective agents for providing visceral pain analgesia in the prehospital setting. While MTX provided a more rapid onset of pain relief, INF provided superior analgesia after subsequent doses and in female, cardiac and older patients.

INTRODUCTION

A variety of prehospital analgesic agents have been used by emergency care practitioners for many years, but they share the common feature of paucity of literature regarding safety, efficacy and relative efficiency.[1]

In Australia, the most frequently used analgesic agent in ambulance practice is Methoxyflurane (MTX), administered by First Aid, Volunteer and Paramedic Ambulance personnel. Opioids are authorised for use by all paramedics in some services and selected officers in others. In Western Australia all paramedics are also authorised to administer intranasal Fentanyl (INF) and its use is increasing across ambulance services in Australia. INF is becoming increasingly popular in paediatric emergency medicine in Australasia in preference to intravenous Morphine.[2 3]

Although these agents are well established in local ambulance and military practice, they are not widely used elsewhere in the world with few reports regarding efficacy and safety.[4 5] The aim of this study was to analyse the analgesic effect and changes in vital signs associated with administration of MTX and INF in the prehospital management of pain of presumed visceral origin in Western Australia, and to explore whether combined use is advantageous.

MTX is a volatile, fluorinated hydrocarbon used for analgesia in paediatric and adult patients since the 1960s.[6] Reports have questioned its safety due to dose-dependent nephrotoxicity for longer-term analgesia[7] and anaesthesia,[8] particularly when used in conjunction with known nephrotoxins.[9] MTX has been used routinely in subanaesthetic doses by ambulance services Australia-wide for prehospital analgesia for more than three decades at doses lower than those reported above where adverse events have been observed. The Therapeutic Goods Administration (TGA) has no reports of renal toxicity despite an estimated three million patient treatments (Medical Developments International, personal communication 2009). Small observational studies report it as a safe and reliable prehospital analgesic when used at analgesic doses for both adult[10] and paediatric patients, with the caveat that it may lead to brief, self-limiting episodes of deep sedation in young children.[11 12] Longer-term follow-up of more than 17 000 patients receiving MTX has shown no increase in adverse events (I Jacobs, unpublished data 2009).

Exposure to anaesthetic gases is measured in parts per million (ppm). Thresholds are described as a time-weighted average (TWA) (the average continuous exposure) and a 'ceiling' level over a single hour, generally cited as four times the TWA.[13]

Exposure Standards have not been established for MTX. Standards for Halothane are accepted as applicable and relevant. The TWA threshold for Halothane as a sole agent (and hence MTX) is 50 ppm.[14] However, in the operating room environment, Halothane is typically administered with nitrous oxide (N_2O) at 50 times the concentration of Halothane. The TWA for N_2O is 25 ppm. Hence, in the operating room environment, the TWA for Halothane is adjusted to 0.5 ppm (and ceiling value 2 ppm) because, although this is 100 times lower than the threshold value for Halothane itself, a level of Halothane of 0.5 ppm would be associated with N_2O at its threshold level of 25 ppm.

An Ambulance commissioned study of MTX exposure found that MTX levels did not reach the 1 h peak of 2 ppm or shift average of 0.5 ppm unless oxygen was administered through the device.[15] Ambulance Services throughout Australia have now changed Practice Guidelines to advise against routine administration of oxygen through the device (see online appendix).

Fentanyl is a potent, synthetic opioid used for analgesia since the 1960s.[16] Previous studies favourably report its safety and efficacy as a prehospital analgesic in both paediatric and adult cases when administered intravenously[17–22] or intranasally.[3 23] Fentanyl has been suggested as the preferred opioid in the prehospital setting[19] due to its rapid pain relief, short duration of action, non-histamine release (a major component contributing to hypotension) and reduced incidence of nausea and vomiting.[16 21 24] When compared for efficacy in the prehospital setting, INF and intravenous morphine are comparable.[23]

Within the Western Australian Ambulance Service, the most commonly used analgesic agents are inhaled MTX, introduced in the 1980s and INF introduced in 2001. Combined use has been reported by paramedics to enhance pain relief. This reported synergism, however, remains to be verified.

METHODS

We undertook a retrospective, observational review of patient care record forms encompassing patients administered MTX or INF for the prehospital management of presumed visceral pain by the Western Australian Ambulance Service between January 2004 and February 2006. For the purpose of this study, visceral pain was determined by attending paramedics as being of cardiac, renal or abdominal aetiology.

Of 14 232 cases available, 10 900 (76.6%) patients received MTX, and 3332 (23.4%) patients received INF. Six hundred cases were randomly selected per drug cohort, with cases coded as abdominal, renal or cardiac pain. One thousand and twenty-four cases had sufficient data for further analysis. Of these, 465 (45.4%) received MTX, 397 (38.8%) received INF, and 162 (15.8%) received both.

MTX is self-administered by patients via a hand-held inhalation device (Penthrox inhaler; Medical Developments International, Springvale, Australia). A single dose of 3 ml delivers MTX at a concentration of 0.2% or 0.4% depending on whether the diluter hole is open or occluded. After an initial loading dose of 10–12 breaths through the device, the patient is encouraged to take a few breaths through the device every few minutes as required thereafter. A single dose will provide analgesia for 15–20 min if oxygen is administered through the device, or up to 1 h if used intermittently (and oxygen administered separately by face mask as required). A second dose may be administered when the initial dose has been exhausted.

INF was administered by attending ambulance officers via a metered dose delivery at a concentration of 300 μg/ml in accordance with the dosing regimen in table 1.

Table 1 Intranasal fentanyl dose regimen

Dose chart		
Age	**First dose**	**Subsequent at 10 min**
<5 years <20 kg	1×0.05 ml (15 μg)	1×0.05 ml (15 μg)
6–10 years 21–30 kg	1×0.10 ml (30 μg)	1×0.10 ml (30 μg) Subsequent at 5 min
11–15 years 31–40 kg	1×0.15 ml (45 μg)	1×0.15 ml (45 μg)
Small/elderly/frail	2×0.20 ml (120 μg)	1×0.20 ml (60 μg)
Adult	3×0.20 ml (180 μg)	1×0.20 ml (60 μg)

The choice of analgesic agent is at the discretion of the attending paramedic. For both agents, administration is continued as needed up to hospital arrival and may be continued at the discretion of receiving hospital staff.

Data extracted from patient records included patient demographics (age, gender, aetiology of pain), vital signs (systolic blood pressure (SBP), pulse rate, respiration rate and Glasgow Coma Scale (GCS) score), and a pain assessment utilising Visual/Verbal Analogue Scale (VAS) pain scores (assessed by paramedics). The limits used to define clinically significant extremes of vital sign measurements are listed in table 2. A 1.4-point change in VAS pain score is considered clinically significant.[25] As VAS pain scores for individual patients are assessed as whole numbers, a change of 2 points was considered clinically significant for an individual patient.

Statistics

Data were exported into and analysed with SPSS (version 11.5: SPSS, Chicago, Illinois). Descriptive statistics and frequencies are reported. A sample size of 600 per drug cohort was calculated to provide 80% power to detect a statistical difference with α set at 0.05. A two-way, repeated-measures analysis of variance (ANOVA) was used to test for significant differences in vital sign means over the measured intervals. The Student t test was used to compare pain score reduction and χ^2 test for proportions with pain score reduction ≥2 points.

RESULTS

Patient demographics

Males (584) represented 57% of the cohort, and most patients (62.3%) were over 50 years of age with a mean age of 59.1 (female 58.7, male 59.4) years (table 3). Pain aetiology was classified by the attending paramedic as cardiac (485, 47.4%), abdominal (249, 24.3%) and renal (290, 28.3%) (table 4).

Physiological vital signs

SBP, pulse rate and respiration rate were recorded at three time points: prior to administration of medication, 5 min after administration and on arrival at hospital. Changes in conscious state were assessed by determining GCS prior to and 5 min after administration of the analgesic agent.

Blood pressure

Changes in SBP 5 min after initial analgesic dose varied considerably for individual patients (range −170 mm Hg to +70 mm Hg). Despite these large individual variations, the majority of changes were towards the normal range. Only four patients with initial SBP>100 mm Hg entered the hypotensive range (SBP<90 mm Hg). Three received INF as sole therapy for cardiac pain, and one patient received both for abdominal pain.

The reduction in mean SBP 5 min after the initial dose of MTX was 5.7 mm Hg (median 10 mm Hg) and after INF was 4.5 mm Hg (median 5 mm Hg) (table 5). Similar changes were seen on arrival at hospital, with MTX reducing mean SBP by 15.1 mm Hg (median 20 mm Hg) and INF 11.5 mm Hg (median 15 mm Hg).

Table 2 Vital sign parameters classified as clinically significant

Vital sign	Lower limit	Upper limit
Systolic blood pressure (mm Hg)	<90 (hypotension)	>180 (hypertension)
Pulse rate (per min)	<60 (bradycardia)	>100 (tachycardia)
Respiration rate (per min)	<8 (bradypnoea)	>24 (tachypnoea)

Table 3 Age group, gender and agent administered

	Gender and agent									
	Gender unspecified	Female				Male				
Age group (years)	Fentanyl	Methoxy	Fentanyl	Both	Female total	Methoxy	Fentanyl	Both	Male total	Grand total
0 to 29		27	9	6	42	16	11		27	69
30 to 44	1	70	32	16	118	64	27	28	119	238
45 to 59		61	32	15	108	56	61	51	168	276
60 to 74	1	32	40	9	81	72	81	30	183	265
75+	2	36	49	2	87	29	51	5	85	174
Unspecified						2			2	2
Grand total	4	226	162	48	436	239	231	114	584	1024

On hospital arrival, 10 patients with initial SBP>100 mm Hg had entered the hypotensive range. All received INF, nine with cardiac and one abdominal pain. MTX was also administered to the abdominal pain and two of the cardiac pain patients. None of these patients received nitrates or other cardiac medications. Of those who became hypotensive after treatment, no other adverse effects in physiological parameters and no fall in GCS were noted. One patient increased SBP within the hypertensive range after treatment (SBP rise from 180 to 190 mm Hg).

Pulse rate

Pulse rate changes were minimal (table 5). In the majority of cases, both agents affected pulse rate favourably towards normal values, but changes were not significant for either cohort.

Respiratory rate

Assessment of respiration indicated very little effect after administration of either agent (table 5). Overall, mean respiration declined by 1.7 rpm initially and by 2.1 rpm on hospital arrival, with median respiration rates unchanged. No patients became bradypnoeic.

GCS

Changes in GCS were negligible (table 6). Five patients had falls in GCS (maximum two points in a male with renal pain receiving INF), and four patients had increased GCS (maximum four points).

Pain scores

Pain score reduction by VAS was assessed 5 min after treatment and on arrival at hospital (table 7). A further subgroup analysis by agent, gender, aetiology and pain group was also performed (table 8). Transport times were comparable for both agents.

As sole agents, MTX produced the greatest initial pain score reduction (p=0.452), and INF provided greater pain reduction by hospital arrival (p=0.007). While both agents were effective, INF provided a significantly greater pain score reduction for cardiac (p=0.025), female (p=0.020) and age 75+ patients (p=0.006) on arrival at hospital.

Analysis of the proportion of individual patients achieving pain score reductions of two points or greater by hospital arrival showed significantly higher proportions with INF overall (p=0.027) and for the subgroups of cardiac aetiology (p=0.033), female patients (p=0.021), female patients with cardiac aetiology (p=0.044) and for patients aged 45–59 years (p=0.047).

Further analysis of the patients aged 75+ years with cardiac pain showed that the difference between agents was limited to female patients in this subgroup (p=0.003) where MTX appeared to be ineffective (table 8).

Differences in pain score between agents were seen in the age groups <30 years (1.50 reduction), 75+ years (1.41 reduction) and in the subgroup of patients with cardiac pain and aged 75+ years (males 1.16, females 1.99, overall 1.95).

The patient care records in use at the time of the study did not record which agent was administered first, and so this could not be analysed. Combined use of agents was not advantageous.

For the 465 patients administered MTX, a single 3 ml dose was used in 241 patients (51.9%), a second dose was used in 195 patients (41.9%) and 29 (6.2%) received a third dose. The mean total dose of INF administered per patient was 362 μg (median 240 μg; SD±191.74).

DISCUSSION

The objective of this study was to analyse and compare the analgesic effect and changes in vital signs associated with administration of MTX and/or INF for the prehospital management of visceral pain. Both agents proved effective with no bradypnoea.

Only one case increased SBP within the hypertensive range (increase from 180 to 190 mm Hg) which is unlikely to be clinically significant. All cases that experienced a fall in SBP from >100 mm Hg to hypotensive levels received INF either alone or in combination with MTX. However, these patients did not experience any fall in GCS or other evidence of respiratory or cardiovascular compromise. The results concur with previous studies indicating that INF is an agent with good analgesic properties.[2 26–28] While one small study found that the rate of adverse events for patients treated with INF in a prehospital

Table 4 Aetiology, gender and agent administered

	Gender and agent									
	Gender unspecified	Female				Male				
Aetiology	Fentanyl	Methoxy	Fentanyl	Both	Female total	Methoxy	Fentanyl	Both	Male total	Grand total
Abdominal	1	61	52	32	145	37	37	29	103	249
Cardiac	3	107	99	3	209	97	159	17	273	485
Renal		58	11	13	82	105	35	68	208	290
Grand total	4	226	162	48	436	239	231	114	584	1024

setting was more than double that of patients administered with intravenous morphine, these effects were minor and did not reach statistical significance.[23]

MTX as a sole agent was not associated with any adverse physiological effects.

The results of the current study of prehospital MTX and INF indicate both provide effective pain relief. MTX showed a greater pain reduction 5 min after commencement of treatment. INF showed a superior pain reduction on arrival at hospital. The results of this study concur with studies conducted in a hospital environment, which report a mean reduction in VAS pain score of approximately four points.[29 30] The time course of VAS pain score reduction we observed is similar to that in hospital for paediatric patients (1.67 point reduction 10 min postadministration and 2.91 point reduction 30 min postadministration).[31]

The subgroup analysis shows that both agents provide effective analgesia across the range of age, gender and pain aetiology. INF produced greater increases in pain score reduction and proportion of patients with VAS reduction of two or more in the subgroups of cardiac pain, female patients and age 75 years and above on arrival at hospital.

It is reassuring to note that for cardiac aetiology of pain, neither INF nor MTX caused respiratory depression or adverse pulse rate changes. INF administration demonstrated more effective pain relief in this group but was also associated with a small number of cases developing hypotension. These effects do not appear to have been associated with clinical compromise and are reassuring in this particular group who are at greatest risk of cardiovascular compromise from analgesic agents.

This study has demonstrated similar results to that seen when morphine was compared with the fentanyl derivative alfentanil for relief of acute ischaemic-type chest pain in the prehospital environment.[32] More rapid pain relief from alfentanil was noted 15 min after administration. However, while INF provided greater pain relief at arrival at hospital, it is evident that MTX is also an effective analgesic agent. Further analysis of the cardiac patients aged 75 years and above showed INF to be particularly effective and MTX ineffective in this group. However, the actual numbers are small, and caution is advised on interpretation of this result.

Historical analysis of INF dosage administration by St John Ambulance paramedics in Western Australia demonstrates a substantial increase in dose per patient since its introduction in 2001, with the average administration increasing from 180 μg in the initial stages following introduction of the agent (Ford D, unpublished, 2004) to the mean reported here of 362 μg. Following analysis of the pilot period in 2001, the initial dose for adults was increased in 2002 from 120 μg to 180 μg, and ongoing education has reinforced the need to continue administration at the recommended intervals if pain relief is inadequate. Increased experience and comfort with use have also contributed to this increase in total dose per person observed over time. The increased total dose administered per patient since initial use in 2001 to that observed here in 2004, without significant adverse effects, is most likely reflective of previously inadequate doses. This 'oligoanalgesia' is well recognised in the prehospital setting.[33–35]

It should be noted that as the population examined in this study were suffering from visceral pain, they are therefore physiologically distinct from patients with pain of traumatic origin, which has been more extensively studied. This may explain the difference between previous findings of a four-point

Table 5 Changes in physiological parameters by agent used

		Methoxy			Fentanyl			Both			Total		
		Initial	5 min	Hospital	Initial	5 min	Hospital	Initial	5 min	Hospital	Initial	5 min	Hospital
Systolic blood pressure (mm Hg)	Average (95% CI)	138.0 (135.3 to 140.6)	132.3 (129.6 to 135.0)	122.9 (119.4 to 126.3)	137.9 (134.6 to 141.2)	133.4 (130.2 to 136.5)	126.4 (123.3 to 129.5)	137.3 (132.8 to 141.9)	134.8 (130.2 to 139.5)	127.2 (122.2 to 132.3)	137.9 (136.0 to 139.7)	133.1 (131.2 to 135.0)	125.3 (123.2 to 127.4)
	<90	6	5	3	13	12	6	1	1	1	20	18	10
	90–180	426	367	194	346	323	262	145	132	89	917	822	545
	>180	23	21	11	35	35	31	12	12	7	70	68	49
Pulse rate (per min)	Average (95% CI)	85.0 (83.4 to 86.7)	82.4 (80.6 to 84.2)	81.1 (78.7 to 83.6)	86.0 (83.5 to 88.5)	84.3 (81.9 to 86.7)	83.0 (80.3 to 85.6)	82.6 (79.9 to 85.4)	80.2 (77.6 to 82.7)	80.5 (77.6 to 83.4)	85.0 (83.7 to 86.4)	82.8 (81.5 to 84.1)	81.9 (80.3 to 83.5)
	<60	20	19	14	35	35	27	8	8	2	63	62	43
	60–100	354	319	164	280	273	219	131	123	83	765	715	466
	>100	90	71	38	81	80	64	22	21	18	193	172	120
Respiratory rate (per min)	Average (95% CI)	22.3 (21.8 to 22.8)	20.6 (20.2 to 21.0)	20.7 (20.1 to 21.3)	22.2 (21.7 to 22.8)	20.7 (20.2 to 21.1)	19.9 (19.5 to 20.4)	21.6 (20.9 to 22.2)	20.1 (19.6 to 20.6)	19.2 (18.6 to 19.8)	22.2 (21.9 to 22.5)	20.5 (20.3 to 20.8)	20.1 (19.7 to 20.4)
	<12	0	0	0	0	0	0	0	0	0	0	0	0
	12–24	359	313	147	300	293	232	131	124	83	790	730	462
	>24	97	91	68	89	84	75	27	26	17	213	201	160

Table 6 Glasgow Coma Scale before and after treatment

Agent	Glasgow Coma Scale after agent	Glasgow Coma Scale before agent 15	14	13	12	11	Grand total
Methoxy	15	456	2			1	459
	14	1	2				3
Fentanyl	15	380	1				381
	14	2	3				5
	13	1					1
	12			1			1
Both	15	156					156
	14		3				3
Grand total		996	11	1		1	1009

pain reduction for traumatic pain (Ford, unpublished, 2004) compared with a three-point reduction found in this study of visceral pain.[36–38]

The use of MTX has changed since the time of this study. Previously, it was routine practice to administer oxygen through the device. This is now recognised to increase evaporation of the agent into the ambient air, reducing the dose delivered to the patient and limiting analgesia to 15–20 min. The current recommended technique is to administer oxygen via a separate face mask and not through the inhaler (see online appendix). Intermittent use of MTX in this manner allows a single dose to last approximately 1 h, and as a result, the need to refill the inhaler with a second dose is now exceedingly uncommon. The briefer duration of effect with oxygen administered through the device—which was common at the time of the study—may also contribute to the lesser effect of MTX with longer transports and by hospital arrival despite having a greater initial effect. With oxygen flowing through the device, exhaustion of the MTX may not have been apparent to either patient or treating officer and hence analgesic effect removed. Further analysis with the current technique and/or comparison of techniques may yield more information.

Interestingly, there was no significant difference in pain assessment scores of patients who received MTX and INF in combination, relative to INF alone. This is consistent with a previous study[23] that demonstrated similar or less pain reduction when these agents were combined in patients with non-cardiac pain. One possible explanation is that a second agent has been used when the first agent is ineffective, and hence the use of both agents is apparently less as it is a group of relative 'non-responders' or those suffering hyperalgesia. Further studies will be required to examine the sequence and timing of agents and the effect of each individually when used in combination. It is also unknown how frequently both agents were used simultaneously from the outset. Until these issues are clarified, no firm recommendations can be made regarding routine use of both agents.

Limitations

The limitations of the study are consistent with retrospective, observational studies of this nature and relate to available equipment, the study population and compliance with recording procedures.

The investigation of the analgesic agents' effect on respiration has been limited to respiratory rate and GCS. More sensitive indicators are oxygen saturation and end tidal CO_2 ($ETCO_2$) monitoring. However, oxygen saturations were not routinely measured and/or repeated at the time of this study and $ETCO_2$ monitoring in spontaneously breathing patients requires

Table 7 Changes in pain scores by agent used

		Methoxy			Fentanyl			Both			Total		
		Initial	5 min	Hospital	Initial	5 min	Hospital	Initial	5 min	Hospital	Initial	5 min	Hospital
Pain score	Average (95% CI)	8.1 (7.9 to 8.3)	6.2 (5.9 to 6.4)	5.5 (5.1 to 5.9)	7.6 (7.4 to 7.8)	6.0 (5.8 to 6.3)	4.4 (4.1 to 4.7)	8.8 (8.6 to 9.0)	7.0 (6.6 to 7.3)	5.4 (4.9 to 5.9)	8.1 (7.9 to 8.2)	6.3 (6.1 to 6.4)	4.9 (4.7 to 5.2)
Pain reduction	Average (95% CI)		2.0 (1.7 to 2.2)	2.5 (2.1 to 2.9)		1.6 (1.4 to 1.8)	3.2 (2.9 to 3.5)		1.8 (1.5 to 2.2)	3.4 (2.8 to 3.9)		1.8 (1.7 to 1.9)	3.0 (2.8 to 3.2)

Table 8 Pain score reduction at hospital arrival: subgroup analysis of methoxyflurane and intranasal fentanyl use as sole agents

	Gender	Group	No Methoxy	No Fentanyl	Pain reduction on arrival at hospital Methoxy average (95% CI)	Pain reduction on arrival at hospital Fentanyl average (95% CI)	p Value* Pain reduction on arrival at hospital	Numerical Difference in pain reduction	2+ reduction Methoxy no (%)	2+ reduction Fentanyl no (%)	p Value† 2+ reduction
All	All	All	175	273	2.51 (2.14 to 2.88)	3.18 (2.87 to 3.50)	0.007	0.67	113 (65%)	203 (74%)	0.027
Aetiology	All	Abdominal	37	50	2.97 (2.16 to 3.79)	3.81 (3.16 to 4.46)	0.120	0.84	27 (73%)	42 (84%)	0.209
	All	Renal	27	23	2.67 (1.74 to 3.59)	3.24 (2.54 to 3.94)	0.337	0.57	21 (78%)	20 (87%)	0.400
	All	Cardiac	111	200	2.32 (1.85 to 2.79)	3.02 (2.63 to 3.41)	0.025	0.70	65 (59%)	141 (71%)	0.033
Gender	All	Male	76	167	2.51 (1.97 to 3.06)	3.06 (2.68 to 3.45)	0.108	0.55	50 (66%)	121 (72%)	0.291
	All	Female	99	102	2.51 (2.00 to 3.02)	3.40 (2.86 to 3.95)	0.020	0.89	63 (64%)	80 (78%)	0.021
Gender and aetiology	Male	Abdominal	9	26	2.67 (0.94 to 4.40)	3.52 (2.56 to 4.48)	0.413	0.85	6 (67%)	21 (81%)	0.385
	Male	Renal	15	18	3.33 (2.19 to 4.48)	3.47 (2.63 to 4.31)	0.849	0.14	14 (93%)	16 (89%)	0.658
	Male	Cardiac	52	123	2.25 (1.60 to 2.90)	2.91 (2.44 to 3.37)	0.113	0.66	30 (58%)	84 (68%)	0.179
	Female	Abdominal	28	23	3.07 (2.14 to 4.01)	3.96 (3.10 to 4.81)	0.178	0.89	21 (75%)	20 (87%)	0.285
	Female	Renal	12	5	1.83 (0.41 to 3.26)	2.40 (1.62 to 3.18)	0.505	0.57	7 (58%)	4 (80%)	0.394
	Female	Cardiac	59	74	2.38 (1.71 to 3.05)	3.30 (2.60 to 3.99)	0.066	0.92	35 (59%)	56 (76%)	0.044
Age group	All	0 to 29	15	10	2.80 (1.59 to 4.01)	4.30 (3.47 to 5.13)	0.058	1.50	12 (80%)	10 (100%)	0.132
	All	30 to 44	42	36	3.14 (2.41 to 3.88)	3.85 (3.05 to 4.64)	0.206	0.70	32 (76%)	32 (89%)	0.145
	All	45 to 59	45	64	2.12 (1.27 to 2.98)	2.76 (2.17 to 3.35)	0.233	0.64	24 (53%)	46 (72%)	0.047
	All	60 to 74	39	96	2.79 (2.06 to 3.53)	3.11 (2.53 to 3.70)	0.505	0.32	27 (69%)	68 (71%)	0.853
	All	75+	33	67	1.76 (1.03 to 2.48)	3.17 (2.52 to 3.82)	0.006	1.41	17 (52%)	47 (70%)	0.068
Cardiac 75 + years	Male		10	25	2.20 (1.08 to 3.32)	3.36 (2.39 to 4.33)	0.139	1.16	6 (60%)	17 (68%)	0.652
	Female		9	25	0.33 (−0.84 to 1.51)	3.32 (1.97 to 4.67)	0.003	1.99	1 (11%)	17 (68%)	0.003
	Unspecified		0	2	NA	1.50 (−1.44 to 4.44)	NA	NA	NA	1 (50%)	NA
	Total		19	52	1.32 (0.42 to 2.22)	3.27 (2.47 to 4.07)	0.003	1.95	7 (37%)	35 (67%)	0.021

*t Test.
†χ^2 Test.
NA, not applicable.

equipment not currently utilised in ambulance services in Australia. It is possible, therefore, that minor degrees of respiratory depression have not been identified. Similarly, GCS is a crude estimate of conscious status. Confusion and/or disorientation are important effects produced by both these agents but not specifically analysed in this study. Further research is required to assess the significance or otherwise of these factors.

No allowance has been made for the analgesic effect of nitrates and oxygen for patients with pain of presumed cardiac origin. Although the use of these confounders is routine and is assumed to be similar between subgroups, this was not specifically analysed. Similarly, the pathological conditions associated with visceral pain influence the physiological parameters measured making interpretation of changes difficult to determine because of pain, pain relief, underlying condition or combinations of these.

While the study population encompassed all age groups, only 1.1% of patients were under 20 years of age. Paediatric patients are therefore under-represented in this study, and as such we are unable to specifically analyse the effects in this group. Finally, the analysis of patient records was hampered by incomplete data, with missing values attributed to short journey time to hospital and non-compliance with completion of the case sheets by paramedics.

CONCLUSION

The results presented in this paper demonstrate MTX and INF are effective analgesic agents for the prehospital management of visceral pain, with only a very small number of cases in the INF group associated with subsequent hypotension but no change in GCS or other evidence of cardiovascular compromise. No patients were compromised by a fall in consciousness level or impaired respiratory rate. MTX may be the treatment of choice for shorter patient contact cases due to ease of administration, but INF provided superior pain relief at hospital arrival, and achieved greater pain relief for presumed cardiac pain, particularly in older and female patients. No clinical advantage could be detected by their combined use, however measures were limited.

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