SHORT REPORT:

RESULTS of HYDROMORPHONE SURVEY of Palliative Care Physicians within the UK and Ireland

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of Palliative Care Physicians within the UK and Ireland

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Within the western world control of cancer pain is dominated by the use of morphine[1]. There are many formulations available which allow titration of doses until equilibrium is reached to suit the individual patient's needs. Ultimately when a controlled pain state is reached we strive to maintain good pain control for patients with the use of slow release formulations using normal release morphine for breakthrough pain[2,3]. Unfortunately, there are some patients who cannot tolerate the side effects of morphine despite the use of the many adjuvant therapies available to treat undesirable symptoms [4]. The increasing availability of opioids other than morphine provide an alternative approach. In the treatment of this cohort of patients, the concept of opioid switching has developed [5] . It has been found that often patients who cannot tolerate morphine because of side effects can be well controlled on other opioids with fewer side effects in their individual case [6].

Problems arise, however, when these patients reach an advanced stage of their disease and require opioids subcutaneously (SC) via a syringe driver. Their intolerability of oral morphine creates a dilemma as it is likely that they will have similar difficulty with Diamorphine which is metabolized to morphine almost completely. Although there is a parental formulation of Hydromorphone it has not been marketed for use in the UK. Nevertheless, it is possible for palliative care physicians to access supplies from Ireland. At equivalent doses the analgesic efficacy of Hydromorphone is equal to Diamorphine when used as a SC infusion. What is less known is

Hydromorphone's apparent clinical compatibility when mixed with other drugs normally used with SC Diamorphine. The purpose of this survey was to find out which drugs and/or combination of drugs are being used safely with Hydromorphone in a SC infusion.

Survey

A short questionnaire was designed to ascertain which drugs were being used without apparent interaction when mixed with Hydromorphone in a SC infusion. The design of the questionnaire consisted of a table laid out on a single page which was quick and easy to complete by palliative care physicians. In addition there was space for comments to be made and the participants were asked to write their name and address on the back if they wished a copy of the results sent to them. The questionnaires were sent out to those palliative care physicians identified in the Hospice Information Directory of the UK and Ireland, 2002.

Results

310 questionnaires were sent out and 231 (75%) were returned. Nine (4%) questionnaires were returned blank and one participant commented that they had already returned a completed questionnaire. It was felt this was probably the reason for the other eight returned blank as many palliative care physicians work across more than one site i.e hospice and palliative care hospital teams. The remaining 222 (96%) questionnaires returned were evaluable. Of these 23 (10%) participants said they had used Hydromorphone as a S.C. infusion and 199 (90%) had not used it.

When using an additive, the participants were asked if they had encountered any specific problems with precipitation; cloudy appearance; any apparent problem with compatibility i.e. skin reactions and/or dose related problems; and the dilutant used.

Seven physicians who had used Hydromorphone did not complete the rest of the questionnaire, as three had only used it rarely and the other four could not remember what additives they had used ,although they could recall that no problems were encountered. The remaining sixteen physicians reported a range of use from one to ten of the additives Hereafter, the results reported are for the sixteen physicians who completed this part of the questionnaire.

All of the additives were used by at least one of the sixteen respondents, with Midazolam being the most commonly used additive followed by Levomepromazine , Haloperidol and Hyoscine Butylbromide (*Table 1*).

Table 1 here

The dilutant used was water, except with Dexamethasone where 0.9% saline was used. Dexamethasone and Cyclizine appear to be the only additives reported to have problems with precipitation, cloudy appearance and incompatibility. It was not clear from the data how often this had happened and what adjustments were made if any to overcome these problems. There were few reports of skin reactions, but most additives have had at least one with the exception of Dexamethasone, which had none (*Table 2*). This pattern mirrors that seen when the above drugs are mixed with Diamorphine.

Table 2 here

Eight physicians had mixed Hydromorphone in a S.C. infusion with 3 or 4 of the above additives (table 3). All mixtures of 3 or 4 drugs were mixed with water with no apparent evidence of physical incompatibility or of site reactions. Although there were no reports of dose-related problems, it is worthy of note, that one physician stated precipitation is more likely with higher doses of Hydromorphone.

Table 3 here

Discussion

It is surprising that so few Palliative Care physicians responding to this survey used Hydromorphone. Although morphine and hence Diamorphine intolerance is infrequent one would expect more physicians to encounter it and hence have to use SC Hydromorphone.

Some physicians commented that Hydromorphone is difficult to locate in the UK and that they would use it if it was readily available. In Ireland, however, where availability of Hydromorphone is not a problem availability of Diamorphine certainly is a problem. Given that this survey was conducted with palliative care physicians within the UK and Ireland the factor of drug availability should be taken into account when interpreting these results.

This survey was conducted before parental Oxycodone became available.

References

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Tables

Table 1: *No of Physicians who have used a SC Infusion of Hydromorphone with Additive(s)*

No	Additive	**No**	Additive
15 / 16	Midazolam	8 / 16	Hyoscine Hydrobromide
13 / 16	Levomepromazine	7 / 16	Cyclizine
11 / 16	Haloperidol	6 / 16	Dexamethasone
10 / 16	Hyoscine Butylbromide	6 / 16	Octreotide
9 / 16	Metoclopramide	3 / 16	Other (s) ; 1) *Glycopyrronium Bromide*

Table 2 : *No of problems reported with the use of Additive(s)*

Additive(s)	*Precipitation*	*Cloudy Appearance*	No of Skin reactions / No of uses
Midazolam	*No Reports*	*No Reports*	1 / 15
Levomepromazine	*No Reports*	*No Reports*	2 / 13
Haloperidol	*No Reports*	*No Reports*	1 / 11
Hyoscine Butylbromide	*No Reports*	*No Reports*	1 / 10
Metoclopramide	*No Reports*	*No Reports*	1 / 9
Hyoscine Hydrobromide	*No Reports*	*No Reports*	1 / 8
Cyclizine	1 / 7	1 / 7	2 / 7
Dexamethasone	1 / 6	1 / 6	*No Reports*
Octreotide	*No Reports*	*No Reports*	1 / 6
Other: *Glycopyrronium Bromide*	*No Reports*	*No Reports*	*No Reports*

Table 3 : *Additive(s) used in 3 or 4 combinations with Hydromorphone in SC Infusion*

No	*Combination of Additive(s)*	*Precipitation*	*Cloudy Appearance*	*No of Skin reactions / No of uses*
A	*Hydromorphone* + Cyclizine +Haloperidol	*No Reports*	*No Reports*	*No Reports*
B	*Hydromorphone* + Hyoscine Butylbromide + Haloperidol	*No Reports*	*No Reports*	*No Reports*
C	*Hydromorphone* + Midazolam + Haloperidol	*No Reports*	*No Reports*	*No Reports*
D	*Hydromorphone* + Midazolam + Levomepromazine	*No Reports*	*No Reports*	*No Reports*
E	*Hydromorphone* + Hyoscine Butylbromide + Midazolam	*No Reports*	*No Reports*	*No Reports*
F	*Hydromorphone* + Hyoscine Butylbromide + Levomepromazine	*No Reports*	*No Reports*	*No Reports*

NB: *4 drug combinations used with Hydromorphone in SC Infusion was any combination from the list of additives*

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of Palliative Care Physicians within the UK and Ireland

Questionnaires Sent Out = 310 Returned Blank = 9 (4%)
Returned = 231 (75%) Evaluable = 222 (96%)

The reasons given for the nine returned blank questionnaires returned were:

a) No Palliative care Consultant in situ
b) Questionnaire already completed

1. **Do you use Hydromorphone as a S.C. infusion?** YES **23** / 222 (10%)
NO **199** / 222 (90%)

Of the 23 (10%) Palliative Care Physicians who said they had used Hydromorphone as a S.C. infusion, seven physicians could not remember any of the other drugs added although four stated that they could recall the no problems were encountered. Therefore the results on the table below are for the 16 physicians who completed all of the questionnaire on their experience of using the additives.

SC Infusion Hydromorphone	ADDITIVE	RESULTS		*Please circle*	*your responses*	
No of Physicians who have used it with:		*Precipitation*	*Cloudy Appearance*	*Any apparent problem with compatibility*	*If YES Please specify*	*Dilutant used*
8 / 16	Hyoscine Hydrobromide	No 8	No 7	No 7	Skin reaction 1	WATER 7
10 / 16	Hyoscine Butylbromide	No 10	No 9	No 9	Skin reaction 1	WATER 9
15 / 16	Midazolam	No 14	No 13	No 14	Skin reaction 1	WATER 14
13 / 16	Levomepromazine	No 12	No 11	No 12	Skin reaction 2	WATER 11
11 / 16	Haloperidol	No 10	No 9	No 10	Skin reaction 1	WATER 10
9 / 16	Metoclopramide	No 8	No 7	No 8	Skin reaction 1	WATER 7
7 / 16	Cyclizine	Yes 1 No 6	No 5	Yes 1 No 5	Skin reaction 2	WATER 5
6 / 16	Dexamethasone	Yes 1 No 3	Yes 1 No 2	Yes 1 No 2	Skin reaction 0	0.9% Saline 1 WATER 2
6 / 16	Octreotide	No 6	No 5	No 5	Skin reaction 1	WATER 4
3 / 16	Other - please specify	No 3	No 2	No 2	Skin reaction 0	0.9% Saline 1

8 / 16 had mixed Hydromorphone in a S.C. infusion with 3 or 4 of the above.

All mixtures of 3 drugs were mixed with water with no apparent evidence of physical incompatibility or of site reactions. Although, it is worthy of note from one physician who stated that precipitation can occur with higher doses of Hydromorphone.

Some physicians commented that Hydromorphone is difficult to locate in the UK and would use it if was readily available. In Ireland, however, where availablility of Hydromorphone is not a problem availablility of diamorphine certainly is a problem. Given that this survey was conducted with palliative care physicians within the UK and Ireland the factor of drug availability should be taken into account when interpreting these results .

Palliative Medicine

Authorship

We the undersigned have read and agree with the final content of this paper.

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