

INTRAVENOUS FLUIDS IN MEDICAL IN-PATIENTS

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1 Data from the Boston Collaborative Drug Surveillance Program were reviewed to determine the proportion of patients receiving intravenous fluids in the participating hospitals.

2 Wide differences between hospitals in the United States and four other countries were observed: i.v. fluids being given to 54% of patients in one American hospital and only 7% of patients in an Israeli one. A two-fold difference in the frequency of i.v. fluid use in two otherwise comparable Scottish teaching hospitals was observed. This difference was not due to observed patient characteristics, did not arise from selection bias or observational differences between the two hospitals and was unlikely to have arisen by chance.

3 It is concluded that the findings were due to different policies on the part of the attending physicians. Although the study could not be used to evaluate the beneficial effects of the administered fluids, adverse effects were common (15% of recipients) and in some instances potentially serious. Adverse effects were reported more frequently after infusion of 5% dextrose (13% of recipients) than after isotonic saline (7%) perhaps because of the low pH of the former solution.

Introduction

A routine screening analysis of data from a comprehensive drug surveillance programme revealed a marked disparity in the use of intravenous fluids in the medical wards of two otherwise comparable teaching hospitals. The present paper reports a detailed investigation of this finding, describes the use of i.v. fluids in these wards, and reports the frequency of adverse reactions attributed to them.

Methods

The Glasgow Drug Surveillance Programme collects data on consecutive admissions to selected medical wards in two major teaching hospitals of the University of Glasgow. The methods of the study are those of the Boston Collaborative Drug Surveillance Program, have been outlined previously (Jick, Miittinen, Shapiro, Lewis, Siskind & Slone, 1970), and will be mentioned only briefly here.

Consecutive patients are interviewed by the trained nurse monitors and information collated from clinical records, the patient and the attending physicians. Patient characteristics recorded include age, sex, height, weight, admission blood urea, protein and haemoglobin levels, a history of drug consumption prior to hospitalization and up to four discharge diagnoses. The nurse monitors attend ward rounds and collect information on all drugs given to each patient, together with a record of whether or not the patient develops any undesired or unintended effect attributed to the therapy. The resulting information is subsequently edited for completeness and correctness and transferred to Boston for entry onto computer files there.

Routine analyses of this information are regularly provided for scrutiny. An early observation has been that the use of intravenous fluids varies widely in patients in different hospitals, there being a marked tendency for patients in American hospitals to receive such fluids more frequently than those in other countries (Table 1). Nevertheless, even within the two Scottish hospitals under review there were marked dif-

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Table 1 Use of i.v. fluids in medical wards of hospitals participating in Boston Drug Surveillance Program

Country	Hospital	Intravenous fluid recipients	
		Number	%
U.S.A.	1	1871	53.7
U.S.A.	2	521	51.4
U.S.A.	3	364	37.5
U.S.A.	4	382	35.9
U.S.A.	5	284	34.1
U.S.A.	6	589	32.0
U.S.A.	7	754	28.1
U.S.A.	8	220	27.9
U.S.A.	9	687	24.7
New Zealand	1	260	22.7
Scotland	1	156	16.2
New Zealand	2	30	14.0
Israel	1	61	12.9
Canada	1	134	8.1
Scotland	2	71	7.8
Israel	2	176	7.4

ferences in the frequency of intravenous fluid administration. This finding has remained constant throughout the study and is explored in more detail in the present report.

A total of 1,872 Scottish patients have been monitored to date. The primary discharge diagnosis was of cardiovascular disease in 36% of patients, gastrointestinal disease in 12%, respiratory disease in 11%, endocrine disease in 8%, cancer in 7% and others in 26%. A total of 909 patients were studied in hospital A and 963 in hospital B. A comparison of patient characteristics and drug usage in the two hospitals is given in Table 2 and of individual drugs given to these patients in Table 3.

Results

A total of 71 patients in hospital A received i.v. fluids during admission (7.8%) compared with 156 in hospital B (16.2%) ($\chi^2 = 30.9$, $P < 0.01$). Factors explored as possible confounding variables

Table 2 Comparison of patients in hospitals A and B

Patient characteristics	Hospital A	Hospital B
Number	909	963
Mean age (years)	57.7 ± 0.6	54.9 ± 0.6
Mean blood urea nitrogen (mg/100 ml)	24.4 ± 0.7	22.3 ± 0.6
Mean duration of hospitalization (days)	15.5 ± 0.5	11.9 ± 0.3
Proportion male (%)	54	49
Mortality (%)	9.0	6.4
<i>Drug administration</i>		
Mean number drugs consumed regularly prior to hospitalization	2.1 ± 0.1	2.4 ± 0.1
Mean number drugs given in hospital	4.5 ± 0.1	4.5 ± 0.1

Results expressed as mean ± s.e. mean.

Table 3 Comparison of drug use in hospitals A and B

Drug	Hospital A		Hospital B	
	Number	%	Number	%
Nitrazepam	270	29.7	287	29.8
Potassium chloride	247	27.2	278	28.8
Frusemide	198	21.8	224	23.2
Ampicillin-amoxycillin	170	18.7	164	17.0
Diazepam	146	16.1	147	15.3
Digoxin	138	15.2	179	18.6
Paracetamol	118	13.0	121	12.6
Pentazocine	101	11.1	79	8.2
Blood transfusion	75	8.3	72	7.5

which might explain the association between fluid use and hospital included sex, survival, age in decades, presenting blood urea concentration (≤ 8 mmol/l, $8 +$ mmol/l) and first discharge diagnosis. None of these factors accounted for the observed association since although there were variations in the frequency of i.v. fluid use within each category, in all situations the use was higher in hospital B than in hospital A (Tables 4 and 5). Whereas the hospitals were comparable with respect to the actual fluids prescribed (Table 6),

each preparation was given more frequently in hospital B than hospital A.

A total of 77% of recipients in hospital A and 75% in hospital B had commenced intravenous fluids within 48 h of hospitalization. Only 4% of recipients in either hospital commenced i.v. fluids later than the seventh day of admission. Thus the hospitals were comparable with respect to the day of first i.v. fluid administration.

The mean volume of fluids infused was greater in hospital A ($5,470 \pm 690$ ml), than in hospital B

Table 4 Effect of potentially confounding variables on association between i.v. fluid use and hospital

Variable	Hospital A		Hospital B	
	Frequency	%	Frequency	%
Male	37/491	7.5	69/468	14.7
Female	34/418	8.1	87/497	17.6
Survived	56/827	6.8	125/901	13.9
Died	15/82	18.3	31/62	50.0
Blood urea				
< 8 mmol/l	30/591	5.1	74/668	11.1
8 + mmol/l	39/258	15.1	71/205	34.6
Age < 49 years	23/253	9.1	41/330	12.4
50-59 years	9/162	5.6	29/191	15.2
60-69 years	20/248	8.1	33/223	14.8
70+ years	19/246	7.7	53/219	24.2

Table 5 Effect of potentially confounding variables on association between i.v. fluid use and hospital

Discharge diagnosis*	Hospital A		Hospital B	
	Frequency	%	Frequency	%
Cardiovascular disease	26/468	3.4	62/430	14.4
Respiratory disease	11/172	6.4	26/183	14.2
Endocrine disease	11/145	7.6	22/121	18.2
Gastrointestinal disease	22/128	17.2	58/209	27.8
Neurological disease	9/119	7.6	11/89	12.4
Haematological disease	2/106	1.9	18/68	26.5

* Patients may have several discharge diagnoses. Classification according to international classification of diseases.

Table 6 Intravenous fluid preparations used

Drug	Hospital A		Hospital B	
	Number	%	Number	%
Isotonic saline	67	7.4	148	15.4
5% dextrose	58	6.3	109	11.3
Half-isotonic saline	0	0	14	1.5
5% laevulose	2	0.2	10	1.0
5% dextrose in saline	1	0.1	7	0.7
Quarter-isotonic saline	1	0.1	1	0.1

(4,910 ± 390 ml). Likewise the commonest volume infused was greater in hospital A (3,000 ml) than in hospital B (1,000 ml).

Adverse reactions to i.v. fluids were relatively common and occurred with approximately equal frequency in hospitals A (9/71 = 12.7%) and B (24/156 = 15.4%). They were not related to age, sex, presenting blood urea concentration or primary discharge diagnosis. In general, reactions were more commonly attributed to 5% dextrose infusion (21/167 = 12.6%) than to isotonic saline (16/215 = 7.4%) although the results did not attain conventional levels of statistical significance ($\chi^2 = 2.83$, $P < 0.1$). Those attributed to normal saline included fluid extravasation (four patients)—thrombophlebitis (twelve patients)—and local pain and discomfort (nine patients), and those attributed to 5% dextrose included fluid extravasation (seventeen patients) and thrombophlebitis (seven patients). The overall frequency of fluid extravasation reported in patients receiving i.v. fluid therapy was 21/227 = 8.9% and of infusion-associated phlebitis was 12/227 = 5.3%. The average duration of i.v. fluid therapy prior to the development of an adverse effect was similar in both hospitals (3.5 days), as was the average volume of fluid infused prior to the reaction (3.4 l).

No patients developed septicaemia or congestive cardiac failure while receiving i.v. fluid therapy.

Discussion

Intravenous fluids are amongst the most commonly prescribed drugs in hospitalized medical patients. In a recent report from the Boston Collaborative Drug Surveillance Program, Miller (1973) observed that 32% of over 8,000 patients in American medical wards had received 5% dextrose during their hospitalization. This rate of i.v. fluid administration far exceeds that observed in the Scottish hospitals studied here, and conceals a wide range of usage patterns even within the American hospitals (24–54% of patients receiving i.v. fluids). Nevertheless, this finding is compatible with a previous study which reported a substantially greater overall drug use in American patients than in a suitable matched group of Scottish patients (Lawson & Jick, 1976).

Of considerable interest is the variation in i.v. fluid use in the two Scottish hospitals studied. It is unlikely that this difference arose by chance in view of the strong statistical significance of the observed association. Of potential confounding factors that might explain the association, age, sex,

discharged diagnosis, presenting blood urea concentration and survival have been ruled out as individual factors although the combined effect of these was not controlled by multivariate analysis. However, on the basis of the figures described here it would seem unlikely that the association could have resulted from confounding factors which were measured in this study. It is unlikely that the association arose as a result of selection of cases for hospitalization. Most admissions to the study wards are of an emergency nature and both hospitals serve as district general hospitals for their respective areas. The great similarity both in other drug use and in the use of blood transfusion is impressive and again argues strongly against a bias of patient selection. Likewise these figures strongly argue against observational differences as a cause of the association. Thus, it seems likely that the observed difference in the use of i.v. fluids in the two hospitals is due neither to chance, confounding, selection bias or observation bias, but rather to different policies with regard to i.v. fluid use. This view is supported by the finding of a greater average volume of fluid infused by physicians in the hospital which used i.v. fluids in fewer patients. While the information available does not permit judgements concerning the beneficial effect of the intravenous fluids, it does indicate that adverse effects attributed to i.v. fluids are not rare phenomena, and implies that the number could be reduced by more selective use.

In the present report 15% of i.v. fluid recipients developed one or more undesired effects attributed to their use, the most frequent effects being fluid extravasation, pain and thrombophlebitis.

The finding of a higher frequency of complications attributed to dextrose solutions than saline is as anticipated. Thrombophlebitis occurs most frequently after dextrose infusions and appears to be related to the low pH of these solutions (Page, Raine & Jones, 1952; Elfving & Saikku, 1966; Clementson & Mosfeghi, 1969). This report has been confirmed by Fonkalsrud, Pederson, Murphy & Beckerman (1968) who reported that the use of buffered dextrose solutions resulted in a reduced frequency of infusion thrombophlebitis. By contrast, Wing (1971) incriminated a degradation product of dextrose arising as a result of sterilization (5-hydroxymethylfurfural) rather than low pH as the aetiological factor. Commercially available 5% dextrose solutions have a pH of between 3.5 and 5.5 (British Pharmacopoeia, 1973), an advantage apparently, from the viewpoint of prevention of caramelization of the solution during sterilization, but a disadvantage from the viewpoint of potential

hazard to the patient. It would appear that knowledge of the low pH of dextrose solutions is insufficiently widespread, and could be increased by recording this on the bottle.

The overall reaction rate in these hospitals is similar to that reported by Riyami (1968) who investigated 250 consecutive infusions and reported a 14% adverse reaction rate. Reactions were most commonly related to duration of therapy, patients receiving therapy for over 72 h having the highest rate. Others have recorded an even greater frequency of unintended effects, Gray (1967) reporting that only one third of intravenous infusions were free of some undesired effects and that the latter were strongly related to the duration of treatment.

Bacterial contamination of intravenous fluid administrations sets is common (Banks, Yates, Cawdrew, Harris & Kidner, 1970) but septicaemia from this source appears surprisingly rare although Darrell & Garrod (1969) have reported two patients who died following septicaemia arising in this way. No patients developed septicaemia in the present series. Collins, Brown, Zimmer & Kass (1968) reported that 39% of 213 consecutive i.v. fluid recipients developed thrombophlebitis, that the clinical appearances did not correlate with the presence of infection and that 1.9% of patients developed frank bacteraemia as a result of the infusion. On removing the catheters fully one third had evidence of bacterial infection. Rarer side effects from i.v. infusions include pulmonary thromboembolism from thrombus arising at the infusion site (Labran, 1967), or as a result of

particulate contamination of the infusion fluid (Turco & Davis, 1971).

The results of this study indicate that greater attention should be directed towards devising techniques for reducing the risk of fluid extravasation during i.v. therapy, that dextrose solutions should be prescribed only when specifically indicated since isotonic saline appears less hazardous, and that re-assessment of the indications for i.v. fluids should be made at regular (perhaps daily) intervals with a view to discontinuing such treatment where possible. Whilst the overall use of intravenous fluids in the wards under study at present is substantially less than that seen in the United States, the differences between the two hospitals under review are impressive. Since the adverse reaction rates for i.v. fluids were similar in both hospitals it would seem likely that the overall incidence of i.v. fluid reactions could be reduced by prescribing fluids less often, without at the same time exposing them to greater risk as a consequence.

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