The title of the article

The contribution of intravenous medicines to water and sodium intake in upper and lower gastrointestinal surgical patients

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Keywords

intravenous medicines; water; sodium; normal saline; fluid balance
ABSTRACT

Objective

The quantitative importance of prescribed intravenous medicines to water and sodium intake in routine clinical practice is undocumented, with uncertain influence on clinical outcomes. The present study aimed to redress this issue in surgical patients with gastrointestinal problems.

Research Methods & Procedures

Prescription and administration of intravenous medicines and fluids were retrospectively reviewed for water and sodium over 24-hour periods in 86 patients in upper and lower gastrointestinal surgical wards in two teaching hospitals. Changes over five years were assessed in the same two wards using the same methodology.

Results

Among the 90.7% of patients prescribed intravenous medicines the median (range) intake was 272 (40–2687) mL water/day and 27 (2–420) mmol sodium/day, with no significant difference between hospitals or ward type. In 28.2% of those receiving any infusates the only source of water and sodium was intravenous medicines, and in 14.3% the medicines provided more sodium than other infusates. Antibiotics and paracetamol accounted for 58.3% of water and 52.3% of sodium in intravenous medicines. ‘Historic’ data of intravenous medicine-related salt and water intake did not differ significantly from ‘current’ data. The literature suggests clinical outcomes can be modulated by variations in water and sodium intake, are well within the range provided by intravenous medicines.

Conclusions

Intravenous medicine prescriptions, particularly antibiotics and paracetamol, can make substantial and clinically relevant contributions to daily water and sodium intake. They have persisted over time, and should be considered during routine assessment of fluid balance and interventions aiming to improve clinical outcomes.
INTRODUCTION

Water and electrolyte disturbances are common clinical problems in both surgical and non-surgical wards, increasing morbidity, mortality and length of hospital stay (1,2). For example, dehydration can cause confusion, especially in the elderly, hypotension and renal failure. Overhydration can cause poor wound healing, cognitive impairment, delayed gastric emptying, cardiac/respiratory failure and abnormalities of tissue function, including abnormal liver function tests. Electrolyte abnormalities can also cause a wide range of effects including confusion, weakness, cardiac arrhythmias, and sudden death. In view of their importance, many studies have examined the effects of water and electrolyte imbalances on clinically relevant outcomes in both surgical and non-surgical wards. For example, excess peri-operative intravenous “saline” (0.9% w/v sodium chloride), with its associated positive fluid balance, has been reported to reduce gastric emptying rates, prolong post-operative recovery of gut function and length of stay (3), and to increase complications after major lower gastrointestinal surgery (4). Restricting intravenous water from ~700mL and sodium from ~95mmol was found to be sufficient to offer clinical benefits.

The contribution of IV medicines to fluid and electrolyte provision in routine clinical practice has been neglected despite their potential importance. The intake of fluid and electrolytes can be increased by IV medicines in various ways. For example, IV medicines contain water as an obligatory component, although the exact amount delivered depends on the administration procedure (slow bolus, intermittent infusion, or continuous infusion), dilution of the active drug to ensure stability, reduction of infusate osmolarity (to prevent venous damage from peripheral venous administration), and dilution to avoid toxic drug side effects if administered by via incorrect routes (e.g. vinca alkaloids (5)). Sodium (typically with chloride) is also frequently administered, especially if the IV medicine is formulated as a sodium salt, or if sodium is required either as an excipient or diluent. With so many different doses and types of prescribed IV medicines, prepared and delivered in different ways, their contribution to total fluid and sodium intake is likely to be variable, and potentially substantial. The proportion of water to sodium may also vary and impact on fluid and electrolyte concentrations and/or balance.

Although these considerations are of obvious relevance to fluid and electrolyte balances and to the clinical care of patients, the quantitative importance of IV medicines has been inadequately investigated. Indeed, several reported studies (3,4) examining fluid and electrolyte balances do not take this source of intake into consideration, implying a variable and uncertain underestimation of fluid and electrolyte intake. There is also uncertainty whether IV medicine contribution to fluid and electrolyte intake varies substantially within and between different types of wards, and whether it has changed over time.

The aims and novelty of this study on surgical wards concerned the following: establishment of the frequency of IV medicine use, the potential range of water and sodium provided by IV medicines, trends over time in the same type of ward, and to consider the clinical implications.
MATERIALS AND METHODS

Overview

One upper and one lower gastrointestinal surgical ward were studied at each of two large UK teaching hospitals (Oxford and Southampton, designated as hospitals A and B respectively) between September 2017 to November 2017 (designated as ‘current practice’). Each was a tertiary referral hospital (~1200 beds) for gastrointestinal surgical problems. To examine trends over time, the results obtained from upper and lower gastrointestinal surgical wards in hospital B were compared to those obtained five years earlier from the same wards using the same methodology (designated as ‘historical practice’). All prescribed IV medicines and IV infusion fluids were assessed on a single day for males and females, from midnight to midnight after excluding all non-surgical and outlier patients, and those prescribed IV nutrition.

Methods

The total amount of water (mL) and sodium (mmol) prescribed and administered over the preceding 24-hour period was calculated from the prescription charts and any other records of IV fluid and medicine administration, including fluid balance charts.

All prescribed IV medicines for the same 24-hour period were included, except for the following, which have negligible/very small contribution to salt and water intake: ‘once only’ opiate doses and associated doses of naloxone ‘if required’; analgesics provided as part of patient controlled analgesic regime; and other low volume variable rate infusions, including sliding scale insulin. Any specific administration instructions on the prescription were assumed to have been followed. In the absence of specific instructions two assumptions were made. First, it was assumed that all IV medicines were administered individually, even if they could have been safely mixed prior to, or during, administration (applicable only to metronidazole and cefuroxime in this study). Second, any individual source of sodium below 1mmol per dose was ignored.

To calculate the minimum and maximum water and sodium that could have been provided by each IV medicine dose prescribed, the latest versions of the ‘Summary of Product Characteristics’ from the Electronic Medicines Compendium (6) and the British National Formulary (7) were used, in that order of preference. In the event that the sodium content of an IV medicine could not be identified from these sources the information was obtained directly from the medical information department of the relevant manufacturer.

The UK reference nutrient intake (RNI) for sodium (for healthy subjects) (8) and the mid-point of a typical clinical guide for total daily water provision for adult surgical patients (9) were used as referents.

Statistics

Comparisons of characteristics between hospital patient groups were undertaken using independent samples t-tests and Chi-Square tests. The Wilson method (10) was used to obtain point estimates and 95% confidence intervals for the rates of different types of IV access. The Chi-Square or Fisher’s Exact test was used to examine the proportion of patients prescribed and given IV medicines. Normality was examined using the Kolmogorov Smirnov tests. The
Mann-Witney U Test was used to examine differences between groups when continuous data were not normally distributed. Analyses were undertaken using SPSS version 24 (SPSS; Chicago, Illinois, USA), and, unless otherwise stated, continuous data are presented as median (range). In all cases statistical significance was set at $P < 0.05$. 
RESULTS

The characteristics of the ‘current’ patient groups from hospitals A and B did not differ significantly (Table 1). The patient characteristics associated with the ‘historical’ data from hospital B (n=43) (mean±SEM; 64.9±2.9 years, 72.3±2.9 kg, 27/43 (62.8%) male; and 22/43 (51.2%) undergoing upper gastrointestinal surgery) also did not differ significantly from those involved in ‘current’ practice in either hospital A or B.

Table 1. Characteristics of the upper and lower gastrointestinal surgical patients (current practice cohort)

<table>
<thead>
<tr>
<th></th>
<th>Hospital A</th>
<th>Hospital B</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>45</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>Sex (proportion male)</td>
<td>26/45 (57.8%)</td>
<td>27/41 (65.9%)</td>
<td>0.442</td>
</tr>
<tr>
<td>Age in years (mean±SEM)</td>
<td>59.8±2.5</td>
<td>65.3±3.2</td>
<td>0.183</td>
</tr>
<tr>
<td>Weight in kg (mean±SEM)</td>
<td>75.5±2.3</td>
<td>79.9±4.7</td>
<td>0.408</td>
</tr>
<tr>
<td>Ward type (proportion in upper gastrointestinal surgery wards)</td>
<td>21/45 (46.7%)</td>
<td>22/41 (53.7%)</td>
<td>0.517</td>
</tr>
</tbody>
</table>

* Chi-Square test for comparisons between proportions and independent samples t-test for comparisons between means.

In hospital A (n=35 of the 42 patients given IV medicines) 25.7% of patients had central venous access (n=9, 95% CI 14.2, 42.1); 45.7% had peripheral venous access (n=16, 95% CI 30.5, 61.8), 5.7% had both central and peripheral venous access (n=2, 95% CI 1.6, 18.6), and the remaining 22.9% had no access at the time of review (n=8, 95% CI 12.1, 39.0). Data on the distribution of IV catheters were not collected from hospital B.

Proportion of patients prescribed IV medicines

Table 2 shows that the overall proportion of patients prescribed IV medicines in the ‘current’ patient groups was 90.7% (n=86), with no significant difference between hospitals A and B (P=0.470) or between upper and lower gastrointestinal surgery wards (P=1.000). Some of the IV medicines were prescribed in case they were needed (‘as required’ IV medicines) but often were not actually needed, with the result that only 50.0% (39/78) of the patients were administered the prescribed IV medicines. There were no significant differences in this proportion between hospitals or between type of wards, with the exception of patients receiving IV medicines on upper gastrointestinal wards, which was higher (P=0.025) in hospital A (73.7%) than hospital B (35.0%). In 28.2% (11/39) of those receiving any infusates the only source of water and sodium was intravenous medicines. Only one patient (from the upper gastrointestinal ward of Hospital B) received a single dose of intravenous diuretic (20mg furosemide).
Table 2. The frequency with which patients in ‘current practice’ were prescribed and given IV medicines, by type of hospital and ward

<table>
<thead>
<tr>
<th>Prescribed IV medicines</th>
<th>Hospital A</th>
<th>Hospital B</th>
<th>Hospitals A + B</th>
<th>P-value* comparing hospitals A v B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper gastrointestinal surgery</td>
<td>19/21 (90.5%)</td>
<td>20/22 (90.9%)</td>
<td>39/43 (90.7%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Lower gastrointestinal surgery</td>
<td>23/24 (95.8%)</td>
<td>16/19 (84.2%)</td>
<td>39/43 (90.7%)</td>
<td>0.306</td>
</tr>
<tr>
<td>Both ward types combined</td>
<td>42/45 (93.3%)</td>
<td>36/41 (87.8%)</td>
<td>78/86 (90.7%)</td>
<td>0.470</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Given IV medicines</th>
<th>Hospital A</th>
<th>Hospital B</th>
<th>Hospitals A + B</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper gastrointestinal surgery</td>
<td>14/19 (73.7%)</td>
<td>7/20 (35.0%)</td>
<td>21/39 (53.8%)</td>
<td>0.025</td>
</tr>
<tr>
<td>Lower gastrointestinal surgery</td>
<td>11/23 (47.8%)</td>
<td>7/16 (43.8%)</td>
<td>18/39 (46.2%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Both ward types combined</td>
<td>25/42 (59.5%)</td>
<td>14/36 (38.9%)</td>
<td>39/78 (50.0%)</td>
<td>0.111</td>
</tr>
</tbody>
</table>

* Fisher’s Exact Test

In the ‘historic’ group (hospital B), the proportion of patients given IV medicines was significantly higher than the ‘current’ groups from the same hospital in upper (17/20 (85.0%) v 7/20 (35.0%), P=0.001) and lower (17/19 (89.5%) v 7/16 (43.8%), P=0.004) gastrointestinal surgery wards, and the combination of the two (34/39 (87.2%) v 14/36 (38.9%), P<0.001). The proportions were also significantly higher than those in the ‘current’ groups from the other hospital (hospital A) and both hospitals A and B, with the exception of upper gastrointestinal surgery in hospital A (17/20 (85.0%) v 14/19 (73.7%), P=0.451).

Prescriptions of ‘as required’ IV drugs were more plentiful than ‘regular’ IV drugs, but a much smaller proportion of the ‘as required’ drugs were administered to patients in all wards of both hospitals combined (7/120 (5.8%) vs 63/69 (91.3%); P<0.001, Fisher’s Exact Test), as well as in individual wards or hospitals.

Amount of water and sodium used to deliver IV medicines

The amount of water and sodium used to deliver the IV medicines was variable and positively skewed (Kolmogorov Smirnov test P<0.001 for each). There were no significant differences in the amounts delivered between hospital A and hospital B (for volume P=0.718 and for sodium P=0.784, Mann-Whitney U test), or between upper and lower gastrointestinal wards (for volume P=0.835 and for sodium P=0.686, Mann-Whitney U test). In addition, there was no difference between the distribution of water or sodium administered from IV medicines between hospitals A and B (for volume P=0.537 and for sodium P=0.226, two-
sample Kolmogorov-Smirnov test), or between upper and lower gastrointestinal surgical wards (for volume \( P=0.995 \) and for sodium \( P=0.765 \) respectively). Therefore, the quantities of water and sodium used to administer the IV medicines for ‘current’ patients in hospitals A and B were combined (n=39 patients), and shown diagrammatically as cumulative frequency polygons (Figures 1a and 1b). For water, the median daily intake was 272mL (corresponding to a cumulative frequency of 50%) with an associated range of 40–2687mL (corresponding to the first (0%) and last (100%) points of the cumulative frequency distribution). For sodium, the median and range were 27 (2–420) mmol. Both Figures 1a and 1b show three additional features. First, the dotted lines indicate the variability that would have occurred if the IV medicines had been administered in the minimum (left of the solid line) or maximum (right of the solid line) of ‘allowed’ amounts of water or sodium. For example, at a cumulative frequency of 50% the variability in water intake from this source is (median (minimum–maximum)) 272 (185–343) mL, whilst at 100% it is 2687 (740–4635) mL. The corresponding figures for sodium are 27 (10–43) mmol and 421 (132–709) mmol. Second, Figures 1a and 1b show an extra solid line corresponding to another potential source of variability: the amount of water and sodium that could have been used to deliver the drugs, if all of the ‘as required’ drugs had actually been administered. With this additional source of intake, the total water administration would have amounted to 476 (3–3483) mL and the total sodium administration to 51 (3–518) mmol (n=39 patients). For simplicity and clarity these additional solid lines of median intake are not accompanied by dotted lines representing the potential minimum and maximum intakes. However, at a cumulative frequency of 50% the values are 476 (323–706) mL for water and 51 (29–81) mmol for sodium and at 100% 3483 (1166–5800) mL and 518 (164–873) mmol respectively. Third, the graphs indicate the daily healthy ‘requirements’ of water (9) and sodium (8) as referents. In the case of sodium (RNI, 70 mmol per day for males or females aged ≥16 years (8)) 38.6% of the RNI was met by administration of IV medicine, 88.8% of patients received more than a quarter of the healthy daily ‘requirement’, 18.5% received more than the RNI, and a few several times more than the RNI. In the case of water, for which the recommended healthy daily intake for adult surgical patients (‘requirement’) is 30mL per kg (9) or 2163±63 mL for subjects weighing 72.1±2.1kg’ – the mean weight±SEM of the group –12.6% of the ‘requirement’ was met by administration of IV medicine. More than half of medicine-related IV water (58.3%) and sodium (52.3%) was due to administration of antibiotics (various) and analgesics (paracetamol), given to 79.5% (n=31/39) of patients.
Figures 1a (water, on left) and 1b (sodium, on right). Cumulative frequency distribution of prescribed and administered water and sodium in a 24-hour period from IV medicines to gastrointestinal surgical patients (n=39). The daily ‘requirements’ of 2163mL water (30mL/kg) and 70mmol sodium for the study group are indicated as referents. In each graph the dotted line on the left indicates the amount of water or sodium that can be given if the IV medicines had been infused with the minimum permissible amount of water or sodium, the dotted line on the right indicates the maximum amount, and the solid line between them, the average of the two. The additional right-sided solid curve on each graph (without minimum and maximum amounts) indicates the average that would have been used if all the ‘as required’ drugs had also been administered.

The ‘historical’ data of the amount of water (355 (6–2579) mL, n=34) and sodium (2 (0–314), n=34) used to administer IV medicines did not differ significantly from ‘current’ group in the same hospital (hospital B). They also did not differ significantly from the ‘current’ group in hospital A or the ‘current’ groups from hospitals A and B combined.

Table 3 complements Figures 1a and 1b by providing more detailed information on water and sodium intake from IV medicines and other IV fluid infusions, according to type of hospital and ward. It shows that the overall median intake of water and sodium provided by IV infusions (upper and lower gastrointestinal wards) in the group receiving both IV medicines and IV fluid infusions was about 4 to 5 times more than that provided in the group receiving IV medicines and no other infusions (P<0.001). In contrast, the intake from IV medicines in the group receiving both IV medicines and IV fluid infusions was 81.8% of the water and 72.7% of the sodium administered to the group receiving only IV medicines (P<0.001 in each case). Despite this, IV medicines in this group (n=28) accounted for the delivery of more water than all other infusions in 3.6% of patients (n=1) and more sodium in 14.3% of patients (n=4) if the maximum possible amounts of water and sodium from IV medicines had been given.
Table 3. The daily quantities of water and sodium given to patients in ‘current practice’, by type of ward and type of IV infusion

<table>
<thead>
<tr>
<th>Patients receiving IV medicines only (no infusions)</th>
<th>Patients receiving both IV medicines and IV fluid infusions</th>
<th>P-value* for IV medicines v IV fluids†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (range) (n patients)</td>
<td>Median (range) (n patients)</td>
<td></td>
</tr>
<tr>
<td>From IV medicines</td>
<td>From IV medicines</td>
<td>From IV medicines and IV fluid infusions</td>
</tr>
<tr>
<td>Water (mL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper gastrointestinal surgery wards</td>
<td></td>
<td></td>
</tr>
<tr>
<td>343 (22–2610) (n=8)</td>
<td>294 (75–840) (n=13)</td>
<td>1674 (700–3455) (n=13)</td>
</tr>
<tr>
<td>Lower gastrointestinal surgery wards</td>
<td></td>
<td></td>
</tr>
<tr>
<td>352 (297–495) (n=3)</td>
<td>220 (50–808) (n=15)</td>
<td>1635 (304–2629) (n=15)</td>
</tr>
<tr>
<td>Upper and lower gastrointestinal surgery wards</td>
<td></td>
<td></td>
</tr>
<tr>
<td>352 (22–2610) (n=11)</td>
<td>288 (50–840) (n=28)</td>
<td>1655 (304–3455) (n=28)</td>
</tr>
<tr>
<td>Sodium (mmol)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper gastrointestinal surgery wards</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 (3–385) (n=8)</td>
<td>21 (3–147) (n=13)</td>
<td>131 (19-298) (n=13)</td>
</tr>
<tr>
<td>Lower gastrointestinal surgery wards</td>
<td></td>
<td></td>
</tr>
<tr>
<td>47 (21–76) (n=3)</td>
<td>24 (4–106) (n=15)</td>
<td>177 (52-368) (n=15)</td>
</tr>
<tr>
<td>Upper and lower gastrointestinal surgery wards</td>
<td></td>
<td></td>
</tr>
<tr>
<td>33 (3–385) (n=11)</td>
<td>24 (3–147) (n=28)</td>
<td>145 (19-368) (n=28)</td>
</tr>
<tr>
<td>P-value* (upper v lower gastrointestinal surgery wards)</td>
<td>0.776</td>
<td>0.786</td>
</tr>
</tbody>
</table>

* Mann-Witney U test
† all comparisons for either water or sodium from IV medicines alone v the same (water or sodium) from IV medicines plus IV fluid infusions for either ward type or both ward types combined are P < 0.001

Figure 2 shows the wide variability in sodium concentrations that can exist in IV medicines, encompassing and exceeding the concentration range 0-154mmol/L found in commonly used infusates, such as 5% w/v glucose and 0.9% w/v saline. The typical concentration of IV
medicines is expected to be in the range 70-140mmol/L, but in individual patients it could potentially range from 0 to 232mmol/L.

Figure 2. Cumulative frequency distribution of the sodium concentration in IV medicines administered over a 24-hour period to gastrointestinal surgical patients (n=39). The lower dotted line indicates the minimum concentration of sodium (calculated from the minimum permissible quantity of sodium and the maximum volume of water), the upper dotted line the maximum concentration of sodium (calculated from the maximum permissible quantity of sodium and minimum volume of water), and the central solid line the average of the minimum and maximum. The sodium concentrations of four commonly used ‘maintenance’ intravenous fluids are also indicated. [Abbreviations: D5W = 5% w/v glucose; D4S = 4% w/v glucose and 0.18% w/v sodium chloride; D5S = 5% w/v glucose and 0.45% sodium chloride; CSL = compound sodium lactate; and NS = 0.9% w/v sodium chloride.]
DISCUSSION

This study shows IV drugs containing water and/or sodium are prescribed for as many as 9 out of 10 of patients on gastrointestinal surgical wards, although only 5 out of 10 patients actually received them since ‘as required’ drugs were often not administered since patients did not ultimately require them. Nevertheless, the intake of water and sodium from prescribed and administered IV medicines can be substantial and clinically relevant to at least some patients. Similarly, since they can be substantial and clinically relevant to at least some patients. Similarly, quantitative contributions of IV medicines to water and sodium intake volumes of IV fluids according to standard practice ~800mL that restriction of the daily IV water intake can be as much as 1013% (709mmol/day, or ~10mmol/kg/day) of the RNI for sodium and 214% (4635mL/day, or ~64mL/kg/day) of the reference water requirement. The intake from this source could be even higher, at 1247% (873mmol, or ~12mmol/kg/day) of the RNI for sodium and 268% (5800mL, or ~80mL/kg/day) of the reference water requirement, if all the prescribed IV medicines were administered. Furthermore, in a small proportion of patients more water and sodium were delivered by IV medicines than by IV infusions, and in about 12.8% (n=11/86) IV medicines were the only source of IV water or sodium. Since oral intake of patients in gastrointestinal surgical wards may be absent, small or reduced on account of the underlying condition(s) and post-operative gastrointestinal status, the intake from IV medicines becomes relatively more important. However, since the variability in water and sodium intake from IV medicines is so large, it would be unwise to treat all individuals as a single entity.

Further insights into the clinical implications of this study can be gleaned by considering the altered salt and water requirements in patients on gastrointestinal surgical wards, and their ability to handle these nutrients in the post-operative period. Since RNIs specifically refer to the requirements of healthy subjects, those of patients with disease may be higher or lower. In patients with high output of gastrointestinal effluents, the requirements of both salt and water can increase considerably. On the other hand, the surgical stress response can impair the body’s ability to dispose of salt and water loads, with adverse clinical outcomes. For example, in patients recovering from surgery for colon cancer (3), it was found that restriction of the daily water intake (from IV and oral routes) to 2320mL water and to 104mmol sodium (from the IV route) during the first 5 post-operative days (1280mL less water and 184mmol less sodium than that provided to the control group according to the prevailing standard practice), was associated with enhanced recovery of gastrointestinal tract function and reduced hospital stay in favour of the group receiving less water and sodium. Another larger study involving colorectal surgery predominantly for cancer (4) also found that restriction of the daily IV water intake to ~1100mL water and ~40-100mmol sodium, or ~800mL less water and ~100-140mmol less sodium than that provided to the control group according to standard practice at the time, reduced a variety of complications. There was also a highly significant dose response relationship between complications and increasing volumes of IV fluids and body weight. From these considerations, it is clear that the quantitative contributions of IV medicines to water and sodium intake should not be ignored since they can be substantial and clinically relevant to at least some patients. Similarly,
measurements or estimates of fluid and salt balances should not ignore the contribution of IV medicines, at least in some groups of patients, which should be identifiable by the treating clinicians and pharmacists. For example, most of the fluid and salt intake from IV medicines was due to administration of paracetamol and various types of antibiotics. A further dimension concerns guidelines and recommendations for the use of IV fluid infusions, including those produced by NICE (11). Since these account for sodium concentration of IV fluid infusions, it may necessary to do the same for IV medicines, especially as this 24-hour study has shown them to potentially vary from 0 to 232mmol/L. Obviously the volume of the infused fluids also needs to be taken into account.

There was no significant difference, between the two hospitals, or between the upper and lower gastrointestinal surgical wards in the patterns of IV medicine prescription and in the distribution of salt and water used to deliver these medicines. This is not surprising since both hospitals were large tertiary referral teaching hospitals. Different results might have been obtained from smaller hospitals, which are likely to manage less complicated problems, perhaps using different policies and different clinical attitudes than tertiary referral hospitals. The data from ‘historic’ practice, 5 years earlier, indicate that although the proportion of patients receiving IV medicines was higher than ‘current’ practice in the same hospital, the amount of water and sodium used to administer the IV medicines did not change significantly. As far as we are aware, this is the first study to examine the contribution of IV medicines to water and sodium intake in hospital wards, which suggests that the potentially large contribution of IV medicines to salt and water intake is not only long-standing, but also probably unrecognised or at least inadequately appreciated.

This study has some limitations. Detailed contextualisation is limited by the lack of information on overall fluid and electrolyte balances, distribution of intake between oral, enteral and intravenous sources, medical instructions for limiting oral (‘fasting’) or enteral intake, and distribution of losses between various sources, such as urine, gastric aspirates and other gastrointestinal effluents, including stoma losses that may require compensation. Another limitation is that the exact contribution of IV medicine-related water and sodium intake is uncertain because the information was not recorded by ward staff. For this reason, estimates were made using maximum, minimum and the average amounts between these two extremes. Yet another limitation is that other sources of variability such as potential mixing of medicines for administration were not documented. However, this would be expected to make little difference to the final results because medicine mixing is typically not undertaken and because it could apply to only limited numbers of medicines. In this study, potential cefuroxime and metronidazole mixing did not apply to any patient from hospital A, and to only 10 doses in 4 patients from hospital B producing a maximum overestimate for the overall cohort of <3% for water (0-2.2%) and sodium (0-2.9%). Other intravenous medicines, such as diuretics, could influence water and sodium requirements, but in this study only one patient received a single (20mg) dose of intravenous furosemide. Finally, care should be taken not to extrapolate the findings of this study undertaken in gastrointestinal surgical wards to other ward types. Therefore, investigations need to be extended to other ward types, preferably with additional examination of the role of IV medicines to deliver other nutrients such as potassium and magnesium. It would also be valuable if such investigations were adequately powered to link observations on sodium and fluid intake from IV medicines with clinical outcomes, taking into account confounding variables, such as type of surgery, comorbidities, age, nutritional status, and composition of fluid infused. The sample size of the present study involving a very heterogeneous group of unselected surgical patients is too small to allow such links to be established with confidence.
In summary, IV medicines can be a variable and clinically significant source of water and sodium intake that should be taken into account when assessing fluid balance and prescribing IV fluids in at least some patients. Introduction of policies to document the volume and type of fluid used to infuse IV drugs in wards or specific groups of patients should be considered.

Declaration of Competing Interest
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Austin and Elia conceived and designed the study, which was developed with input from Joskova and Patkova. Collection and assembly of data were undertaken by Austin, Joskova and Patkova, the main data analyses were undertaken by Austin and Elia, and interpretation of the data was undertaken by Elia, Austin, Joskova and Patkova. The manuscript was drafted by Austin and Elia, and critically reviewed and revised by Austin, Elia, Joskova and Patkova. All authors approved the final version of the manuscript.

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