

A cross-sectional study investigating the relationship between intravenous infusate colonisation and fluid container hang time.

ABSTRACT

Aims. To examine the level of microbial colonisation in intravenous fluids after 24 hours of use in an acute care setting to determine the necessity of changing infusate bags on a time-related basis.

Background. Catheter-related bloodstream infections are a serious and life-threatening complication of intravascular devices. Colonised intravenous fluids are one potential source of infection; however, there is little published literature on incidence rates and few recent studies. Routine intravenous fluid replacement has been advocated as an infection control method, but the effectiveness of this is unknown and the optimal duration for infusate use remains uncertain.

Design. Cross-sectional study over 18 months in a 257-bed teaching hospital.

Methods. Infusate specimens (n=264) were obtained from crystalloid fluids that had been used for 24 hours or more. Microbiological culture and sensitivity testing was performed and infusate-related bloodstream infection rates were recorded. Sample testing of previously unopened intravenous solutions acted as a control.

Results. The infusate colonisation rate was 0.4%, or 0.09 per 1,000 infusion hours. The only isolated organism was coagulase-negative *Staphylococcus*. Infusions had been in use for 24-185 hours (1-8 days). There was no difference in median duration of use for colonised (35.0 hours) and sterile (34.0 hours) specimens (Mann-Whitney test, p=0.99). There were no cases of infusate-related bloodstream infection.

Conclusion. The incidence of intravenous fluid colonisation and the risk of related bloodstream infection are low even after several days of infusate use. Current practice appears to successfully maintain the sterility of intravenous fluids.

Relevance to clinical practice. Routine replacement of intravenous fluids continues in many settings, often 24 hourly, in the belief that this prevents infection. We found no

relationship between duration of use and colonisation and routine replacement may be unnecessary. Further research is needed to investigate the effectiveness of routinely replacing intravenous fluids at set time points to prevent colonisation and infection.

Keywords. Nurses, Nursing, Clinical Trial, Infection Control, Nursing Practice, Evidence-Based Practice.

INTRODUCTION

Intravenous therapy is a vital component of modern healthcare with over 150 million catheters purchased annually in the United States alone (Mermel *et al.* 2001). Infusate colonisation is a rare but potential cause of patient infection and time-limited use of intravenous fluid bags has been proposed as a method of possibly avoiding this risk (CDC 2002). Before 1971, intravenous fluid containers were not routinely replaced, even on catheter resite (Maki *et al.* 1974). Rather, they were used until empty, no longer required, or displayed some malfunction. In 1971, poor quality control during manufacturing saw the release of a large quantity of contaminated fluid bottles, which led to an outbreak of catheter-related infection in the United States (CDC 1971). As an immediate response and before the source of the epidemic was identified, a recommendation to discard intravenous solutions after 24 hours of use was issued in an attempt to prevent or reduce infections and the practice was taken up internationally (CDC 1971). Colonised fluids can certainly lead to infection, but the effectiveness of routinely replacing fluids to prevent this has never been tested. Moreover, despite its weak basis in scientific evidence, the practice of routine fluid bag replacement continues today (Rickard *et al.* 2004).

Modern manufacturing processes are generally thought to be reliable and the more likely risk to patients is from extrinsic (post-manufacture) fluid contamination that may occur when clinical staff connect, or otherwise manipulate, the fluid administration set. However, there is very little published literature on the rate of extrinsic contamination and even fewer recent studies. Early studies of venous infusions in hospital patients reported fluid colonisation rates of 4.9%, 2.8% and 3.3% (Letcher 1972, Amonsén & Gren 1978, Baird & Doery 1981). However, these studies are somewhat irrelevant to today's practice as the materials and methods used for intravenous therapy have changed significantly (for example, plastic fluid

bags rather than glass bottles). A more recent study on fluids from pressure monitoring infusions reported a zero incidence of colonisation in 451 samples (O'Malley *et al.* 1994). The most recent data comes from a study of solutions used in an emergency department where 15.4% of 669 bags were colonised after connection to the administration set but prior to patient connection (Carrasco *et al.* 2004).

The relationship between duration of fluid container 'hang time' and colonisation has been assumed to be positively correlated but this is not supported by research. Prior studies have shown colonisation can occur early, within 12 hours of connection to the patient (Letcher 1972), or even before connection (Carrasco *et al.* 2004). Others have observed no significant relationship between hang-time and colonisation at periods of up to 72 hours of use (Maki *et al.* 1974, Carrasco *et al.* 2004, Amonsens & Gren 1978). Pressure monitoring fluids have been observed to remain sterile even after 96 hours or more of continuous use (O'Malley *et al.* 1994). To our knowledge, there has been no rigorous assessment in the form of a randomised controlled trial to assess the efficacy of routinely replacing intravenous fluid containers as a means of reducing colonisation rates.

In contrast to studies of fluid bags, the relationship between colonisation and the duration of intravenous administration set use (tubing and burettes) has been the subject of much investigation. These studies, including randomised controlled trials and meta-analysis, have supported extending the use for 168 hours or more (Rickard *et al.* 2004, Gillies *et al.* 2004). Therefore, abundant evidence attests that administration sets need to be changed infrequently or never, but intravenous fluid bags continue to be ritually discarded and replaced at frequent intervals in many hospitals. The Centers for Disease Control's 'Guidelines for Prevention of Intravascular Catheter-Related Infections' state that (apart from lipid emulsions and blood

transfusions), no recommendation can be given for the hang time of IV fluids because of the lack of evidence and that this remains an unresolved issue (CDC 2002).

Bloodstream infections may occur secondary to microorganism entry via the catheter-skin tract, the bloodstream (from other infected sites) or infused fluids. Current infection control theory could be described as advocating a 'less is more' approach. That is, the less interruption and manipulation to potential routes of infection (wounds, indwelling devices), the more likely the prevention of microorganism entry. From this perspective, the practice of routinely replacing intravenous fluids, which involves breaking and handling a sterile closed-circuit connected to the patient's bloodstream, seems illogical, even dangerous and thus it is appropriate to assess the efficacy of current practice. Routine replacement relies on the assumption that staff contaminate the bags when connecting them to the administration set and that these microorganisms remain or multiply over time. However, it is plausible that for each colonised bag 'resterilised' by routine replacement, another sterile bag is contaminated during the procedure.

After reviewing current practice and the available literature, we decided to embark on this research study. Our objectives were to document the level of infusate colonisation after 24 hours use and to investigate the relationship between duration of use and colonisation.

METHODS

Setting

This cross-sectional study was undertaken over 18 months at Latrobe Regional Hospital, a 257-bed regional-referral, government teaching hospital in Victoria, Australia. Samples were taken from a critical care unit, a medical ward, a surgical ward and a paediatric/orthopaedic

ward. Before the study, this hospital, unlike others, did not practice routine replacement (except for total parenteral nutrition which was not included in this study). Crystalloid fluid bags were used until no longer required or empty.

Sample

Samples of Baxter Viaflex® (Baxter, Australia) intravenous fluid were obtained from intravenous fluid bags that had been in clinical use for a minimum of 24 hours. All crystalloid fluids without post-manufacturer additives were eligible.

Intravenous fluid bags were initially connected and managed as per normal standard practice. The researchers undertook screening rounds to identify any fluid bags that had been hanging for 24 hours or more, as identified from the patient notes, bag label and discussion with nursing staff. Convenience sampling was used, determined by those days when a researcher was available. Samples could be taken by researchers or staff nurses, all of whom received training in the study procedures. A pre-study pilot trial of the sampling technique was performed to standardise technique and resource material was provided for all staff.

Once a bag was identified as eligible for sampling, the researcher or staff nurse performed a 30-second handwash and disinfected the injection port with a 70% alcohol wipe. After the port was dry, 10mL of fluid was withdrawn in an aseptic manner and mixed by inversion, the needle was removed aseptically and then the syringe contents were dispersed into a sterile specimen jar. Each bag was sampled only once.

In addition, specimens (n=261) were obtained from unused intravenous fluid bags, freshly removed from the sealed manufacturer's packaging, to act as a control and assist with the estimation of contamination rates.

All fluid specimens were subjected to 48-hour microbiological culture and sensitivity testing using blood and MacConkey agar plate in conjunction with cooked meat media incubated in oxygen. Microbiological colony counts and speciation were recorded. Handling of specimens in the laboratory and determination of the outcome measure (colonisation) was undertaken by microbiology staff who were blinded to study group and duration of hang time. Blood cultures were taken if the treating physician suspected a diagnosis of sepsis. Treating physicians were not able to be truly blinded to the duration of fluid bag use because fluid connection times are recorded by nurses in the patient's chart. However, we doubt that physicians had any motivation to calculate hang times and most likely were unaware of this data and of study participation in general. Infusate-Related Bloodstream Infection (IRBSI) was defined as per the CDC definition 'concordant growth of the same organism from the infusate and blood cultures with no other identifiable source of infection' (CDC 2002).

Data Collection

Primary data collected consisted of microbiological results and hours of fluid bag use. Other data included fluid type (glucose, dextrose, etc.), presence of a burette, history of set disconnection (for example, mobile patients who had sets disconnected in between intermittent therapy), usage of bag as a flush device, type of catheter (central, arterial or peripheral line), bag volume and identify of the person who sampled the bag.

Statistics

Power calculations were performed on estimates of colonisation to determine the required sample size based on an anticipated incidence of 2% with a variability of 1%. The Mann-Whitney test was used to compare median hang time between colonised and non-colonised specimens. Risk factors associated with colonised specimens were compared to those of non-colonised specimens using the Chi-square, Fisher's exact test, t-test or Mann Whitney test, as appropriate. A p value of 0.05 was considered significant. SPSS 12.0 (Chicago, USA) was used for all analyses.

Ethics

The study was approved by both the Hospital and the University Human Research Ethics Committees. The requirement for informed consent was waived in consideration of the low risk nature of the study. Positive microbiological results were immediately relayed to the treating medical staff.

RESULTS

Sample

A total of 264 samples were obtained from intravenous fluids in clinical use and the total hang time for the sample was 11,731 hours. Most intravenous fluid bags (77%) were discontinued by 48 hours, 88% by 72 hours, 92% by 96hours, 96% by 120 hours, 98% by 144 hours, 99% by 168 hours and 100% by 185 hours (Figure 1).

All samples were standard crystalloid solutions; predominantly 0.9% Sodium Chloride (normal saline) (n=220, 83%), with the remainder consisting of 5% Glucose, 0.45% Sodium Chloride & 2.5% Glucose, 0.18% Sodium Chloride & 4% Glucose, 3% Sodium Chloride,

Compound Sodium Lactate (Hartmann's), 0.15% Potassium Chloride in 0.18% Sodium Chloride & 4% Glucose Intravenous Infusion (20 mmol KCl/L). Most (61%) samples were from 1000mL bags with the remainder being from 500 mL bags. Almost one third (28%) of specimens were obtained from the Critical Care Unit and the remainder from the general wards. Predominantly, samples (88%) were taken by the three researchers and the remainder by staff nurses.

Incidence of infusate colonisation

Of the 264 clinical samples, seven (2.7%) revealed some bacterial growth. Of these, six specimens were low growth (<5cfu) and one specimen produced 18cfu. Therefore, colonisation (>5cfu) occurred at a rate of 0.4%, or 0.09 per 1,000 infusion hours. All positive specimens were coagulase-negative staphylococcus (dnase negative). There were no cases of IRBSI. One patient had matching blood and infusate cultures, however, there were additional colonised sites and the treating specialist considered the infusate an unlikely source; therefore the criteria for IRBSI diagnosis were not met.

Of the 261 specimens taken from previously unopened intravenous solutions, eighteen revealed some bacterial growth: sixteen specimens of coagulase-negative staphylococcus (cfu<5 n=8, cfu 6-15 n=5, cfu 38-100 n=3) and two specimens of *Aspergillus fumigatus* (both cfu <5). The colonisation (≥ 5 cfu) rate was therefore 3% in the controls.

Relationship between colonisation and duration of bag use

The specimens were taken from infusates that had been in use for 1-8 days, with a median usage time of 34 hours (SD 1.8). The median duration of fluid bag use was not significantly

different ($p=0.99$) between samples that were found to be colonised (34 hours) and those that were sterile (35 hours). The infusate with growth of 18 cfu had been in use for 43 hours.

The only risk variable that was significantly associated with infusate colonisation was lower patient age ($p<0.001$). Patients whose intravenous fluid samples recorded some bacterial contamination were younger (mean 38.3 years) than patients whose samples remained sterile (mean 63.6 years).

DISCUSSION

This study provides a snapshot of the infusate colonisation rate in an acute care hospital, across a diverse sample of patients in medical, surgical, paediatric and critical care settings, receiving commonly used crystalloid fluids. Our finding of 0.4% colonisation is comparable with previously reported rates in other settings of 0%, 2.8%, 3.3% and 4.9% (O'Malley *et al.* 1994, Letcher 1972, Amonsens & Gren 1978, Baird & Doery 1981). We observed a nil incidence of IRBSI; this is also consistent with literature describing this as a rare event (CDC 2002). The current effectiveness of keeping intravenous fluids sterile, in a setting which does not practice routine fluid replacement, has been quantified and appears acceptable.

In this study, we demonstrated that the duration of intravenous fluid bag use was not associated with higher colonisation. This challenges the notion that routine replacement of fluid bags at set time-points is effective in preventing IRBSI. The failure to identify a time-dependent relationship to colonisation is consistent with previous studies in different fluid and patient populations (Maki *et al.* 1974, Amonsens & Gren 1978, Carrasco *et al.* 2004).

Furthermore, our study extends these previous findings which examined fluids in use for up to 72 hours; in this study, fluids were hanging for up to eight days.

Our sample included specimens that may be seen as high risk for infusate colonisation.

Many were attached to burettes, indicating that extra manipulation of the administration set had occurred to attach the burettes and also to deliver multiple intravenous drugs. In addition, many samples were from the critical care unit where patients were more likely to have comorbidities associated with infection risk. Most fluid bags belonged to sets that had been disconnected from the cannula, capped off and hung above the patient's bed, then reconnected to the cannula, often on multiple occasions. This is common in our institution for patients who are mobile and who are not receiving continuous intravenous infusion but who require intermittent antibiotic, or other, infusions. It also occurs, although less frequently, when patients with a low-rate infusion go to the shower. These extra manipulations give opportunities for microbial entry; however, we did not see a higher colonisation in these sub-groups. The finding of significantly higher colonisation rate amongst younger patients is difficult to interpret and may simply be Type I error. This group warrants further investigation.

All contaminated infusate was with coagulase-negative staphylococcus at low counts. While these microbes are commonly implicated in catheter-related infections, they are more usually associated with vascular catheter colonisation than with infusate colonisation (which is typically gram-negative bacilli, or unusual species such as *Enterobacter*, *Serratia marcescens*, *Malassezia furfur* or *Candida parapsilosis*) (CDC 2002, Maki *et al.* 1997, Muder 2001, Horvath & Collignon 2003). We found through our controls that sampler/processor contamination may be as high as 6.7%. This, in addition to the isolation of only coagulase-

negative staphylococci in low numbers, suggests that most, if not all, colonisation was due to researcher contamination, rather than actual colonisation of the fluid containers. There was one occurrence of two colonised samples on the same day (both <5 cfu coagulase-negative staphylococcus and taken by the same sampler), suggesting researcher contamination, although this cannot be known for certain.

We were unable to blind our samplers to hang-time and they may have taken more care with specimens that came from patient bags. Conversely, the laboratory scientists were blinded, which prevented any bias in analysis or reporting. The higher colonisation rate of specimens drawn from sterile, unused bags suggests that the samplers may have taken more care with the clinical samples where they had the potential to harm patients if a non-sterile technique was used. This comparison group allowed us to estimate researcher contamination rate in the clinical specimens. In contrast to our observed 6.9% contamination rate, the only other study to use controls reported a 0% control contamination rate (Maki et al. 1974). We conclude that future researchers need to be mindful of this when designing sampling methods.

If the infusate colonisation was *not* due to researcher contamination, this suggests that intravenous fluids are either not sterile when first opened, or alternately that fluids are contaminated once the containers are used for patient care. In either case, microbial growth appears slow, as we only identified low microbe counts, even in bags that had been hanging for several days. Do these levels pose a risk to patients? We observed no cases of IRBSI which suggests not, although a larger study with thousands of patients would be required to rule out this definitively. Microbiological findings of more dangerous organisms, at higher levels than we observed, would be of greater concern.

Our study challenges the practice of time-limited use of intravenous fluid bags as an infection control strategy. The routine replacement of intravenous equipment involves a risk of contamination because of associated disconnection and manual handling of the formerly closed-circuit (Ducharme *et al.* 1988). It is possible that this practice may *increase* rather than decrease colonisation risk. This study provides a baseline for future randomised controlled trials that are necessary to definitively assess the efficacy of routine replacement of intravenous fluid bags.

To be prudent when advising 'safe' hang times, it should be considered that our sample contained only small numbers used for more than 72 hours. However, we did have a reasonable number of specimens (n=264) that were sampled after at least 24 hours. We found colonisation at this time to be low and it seems reasonable to us to advocate that the current non-evidence based practice of routine replacement at 24 hours should be disbanded, or at least extended.

Clinicians may worry what would happen if hospitals abandoned the routine replacement procedure. When left to natural history to determine when a fluid bag is removed, our data provides some reassurance. Of those bags remaining at 24 hours, most are likely to be removed by 48 or 72 hours anyway, presumably due to the container emptying or therapy ceasing. We believe that it is appropriate to dispense with routine replacement of intravenous crystalloid fluids. If a particular clinical environment or patient mix results in bags hanging for extremely long periods of time, then perhaps time limits, such as 72 hours, or even one week, might be implemented. However, in an acute care hospital, we have shown such policies are unlikely to be necessary.

Savings in financial costs, nursing time and environmental waste could undoubtedly be made if intravenous fluids were not routinely discarded after 24 hours of use. Although there is no definitive evidence in the form of a large randomised controlled trial to support unlimited duration of intravenous fluid use, neither is there evidence to suggest that routine replacement is an effective prevention of infection. While it would clearly be beneficial to remove a colonised bag from a patient's infusion, this situation is likely to happen only rarely. On the other hand, the potential to contaminate fluids during the disconnection/reconnection manoeuvre required for routine replacement could implicate a much higher number of patients. The routine replacement of both central venous catheters and intravenous administration sets are related procedures that were once ritually performed but found to be ineffective when subjected to research investigation (Gillies *et al.* 2004, CDC 2002). It seems that the routine replacement of intravenous fluids is yet another example of a well-meaning, but unfounded, infection control practice that we need to question.

Relevance to clinical practice

Routine replacement of intravenous fluids continues in many settings, often 24 hourly, in the belief that this prevents infection. We found no relationship between duration of use and colonisation, and routine replacement may be unnecessary. Further research is needed to investigate the effectiveness of routinely replacing intravenous fluids at set time points to prevent colonisation and infection.

Limitations

We acknowledge that the conclusions we have drawn from this study are necessarily limited due to the observational design and the conduct of the study in a single centre with a limited

sample size. In particular, the finding of higher incidence of contamination in the fluid bags of younger patients and in the unused bags warrants further investigation. A large multicentre randomised controlled trial with blinded samplers would address these concerns.

CONCLUSION

In summary, this study found a low colonisation rate of crystalloid infusions hanging for at least 24 hours in an acute hospital. There was no relationship between length of time used and likelihood of colonisation, suggesting that routine replacement of intravenous fluid bags at regular time intervals may be unnecessary. This finding supports the current practice at this hospital where we do not limit intravenous fluid hang times for crystalloid solutions. Avoiding routine fluid replacement would result in significant savings in nursing time, financial costs and environmental waste. Reducing the incidence of intravenous fluid bag changes would certainly decrease the potential for contamination of both the fluid and the administration set. Further research is recommended to investigate the effectiveness of routinely replacing infusate fluids at set time points to prevent colonisation.

CONTRIBUTIONS

Study design - CMR BV MRM SR

Data collection and analysis - CMR BV MRM LJK SR CAS GRB

Manuscript preparation - CMR BV MRM LJK SR CAS GRB

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Figure I. Duration of use for specimens sampled

