

# Comparison of normal or heparinised saline flushing on function of arterial lines

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Heparin flushes are widely used throughout health care to help maintain the patency of intravascular devices. This is important for patients, as it reduces the need for the potentially painful process of placing vascular lines, and also helps control costs by reducing the number of devices used for each patient. However, heparin has the disadvantage of interacting with other drugs as well as causing potentially serious side effects.

Evidence supporting the use of alternatives to heparinised saline has been available for 20 years, but it is still used as the flush solution for arterial lines in most New Zealand intensive care units. An informal survey of New Zealand ICUs in 2002 showed that only eight of 26 were using normal saline as their preferred flush solution for arterial lines. Five of those eight were major teaching hospitals.

We undertook a randomised trial to compare the effects of flushing with normal saline or heparinised saline on the function of arterial lines for monitoring and blood sampling.

## Methods

Ethics approval was obtained from the Manawatu–Whanganui Regional Ethics Committee. Consent from patients or their families was waived as both treatments were in clinical use in New Zealand.

All patients (elective and emergency) presenting to the mixed medical and surgical Level 2 ICU of our regional hospital between April and December 2003 were eligible for inclusion in the study. Exclusion criteria were pre-existing coagulopathy precluding heparin use, history of heparin-induced thrombocytopenia, known heparin sensitivity, requirement for therapeutic heparin, and age under 16 years. All patients were given subcutaneous low molecular weight heparin when appropriate.

Arterial lines were 20 cm 20-gauge lines inserted in radial, brachial or femoral arteries (AKS-2020, Smiths Medical Deutschland GmbH, Kirchseeon, Germany). The flushing solution and giving set (TranStar 213 cm, Medex, Dublin, Ohio, USA) were prepared using a 500 mL normal saline bag pressurised to 300 mmHg.

Syringes containing 5 mL of either normal saline or normal saline plus heparin (500 units) were specially prepared by the manufacturer (Baxter Healthcare, Auckland,

## ABSTRACT

**Background:** Heparin is used as a flush solution for intravenous and intra-arterial lines, but has a number of drug interactions, as well as potentially serious side effects.

**Methods:** We compared the function of arterial lines for both monitoring and blood sampling when flushed with either normal saline or saline containing heparin (1 unit/mL). Sixty-five patients were recruited at this mixed medical and surgical Level 2 intensive care unit. Patients were randomised to receive either normal saline (NS) or heparinised saline (HS) (3 mL/hour as a continuous flush). Each patient's nurse was asked to score the function of the line at the end of each nursing shift.

**Results:** 35 patients were recruited in the NS group and 30 in the HS group. Mean study duration was 5.8 and 6.6 days for the NS and HS groups, respectively. The scores for the intravascular line for each patient were summed, and the percentage of the total possible score was calculated. Mean percentage scores were 83% (NS group) and 82% (HS group). Comparison using the central limit theorem showed no difference between the groups at the 95% confidence interval (–6% to 10%).

**Conclusions:** Heparin as a continuous flush at 3 units/hour does not improve the function of arterial lines compared with a continuous normal-saline flush.

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New Zealand). The hospital pharmacy blanked out the manufacturer's labelling, assigned each syringe a random number, and retained the code.

On admission of a patient requiring invasive blood pressure monitoring, a numbered syringe was chosen from the ICU refrigerator. The contents were injected into the 500 mL bag of saline for the flushing solution, which was then attached to the patient's arterial line and delivered as a continuous flush at a rate of 3 mL/h. If the patient required an arterial line for longer than 72 hours, when the giving set would usually be changed, then the pharmacy was asked to provide a further syringe of the same constituents.

At the end of each nursing shift (three per 24 hours), the patient's nurse scored the functioning of the line (3 = functioning well for monitoring and sample-taking; 2 = functioning well most of the time, requires some attention; 1 = functioning poorly; 0 = required changing). Once a line scored 0, the patient was removed from the trial, but the 0 score was continued for every shift for which the patient remained in the ICU after the line failed.

If a line was removed because of lack of clinical need, but the patient remained in the ICU, the line was scored only until its removal.

## Results

Sixty five patients were recruited over 8 months: 35 in the normal saline (NS) group and 30 in the heparinised saline (HS) group. Patient characteristics are shown in the Table.

The study duration was difficult to compare between groups as the data were heavily skewed to a shorter duration. Mean study duration was 5.8 days for the NS group and 6.6 days for the HS group. However, after exclusion of three outliers in each group (beyond the 0–10 day admission range), there was no significant difference in study duration when tested by Students *t* test.

Scores for function of the arterial line for each patient were summed, and a percentage of the total possible score was calculated. The mean percentage scores were 83% for the NS group and 82% for the HS group. These were compared using the central limit theorem. There was no difference between the groups at the 95% confidence interval (–6% to 10%). There was no evidence that the addition of heparin improved the functioning of the arterial line.

Mean daily platelet count and activated partial thromboplastin time (APTT) were also compared using the central limit theorem. Mean platelet counts were  $235 \times 10^9$  cells/L (NS) versus  $257 \times 10^9$  cells/L (HS). These were not different at the 95% confidence interval (–77 to  $37 \times 10^9$  cells/L). APTT values were 40.4 s (NS) versus 37.2 s (HS). These also were not different at the 95% confidence interval (–0.21 to 6.58 s). There was no evidence that heparin at this dose affected platelet numbers or APTT.

## Discussion

Indwelling intravascular lines, such as central venous catheters, arterial lines, peripherally inserted central catheters and dialysis catheters, are now widely used for monitoring and treating critically ill patients. These lines, as well as intravenous cannulas, may be used continuously or intermittently. When not in use, they may be kept patent by flushing with either intermittent injections at regular intervals or low-volume continuous infusions. Heparin-contain-

**Characteristics of patients enrolled in the trial**

Patient characteristics	Normal saline ( <i>n</i> = 35)	Heparinised saline ( <i>n</i> = 30)
Male	18	14
Female	17	16
Mean age (years)	58	50
Mean duration of stay (days)	5.8	6.6

ing solutions are often used for flushing, and the concentration of heparin and volume varies with the type of catheter and with local practice.

Heparin produces conformational, electrostatic and orientation changes in antithrombin III that provide it with more favourable binding to thrombin, thereby producing its anticoagulant effect.<sup>1</sup>

Heparin is incompatible with many drugs<sup>2</sup> and has undesirable effects, the most obvious being haemorrhage, where high doses can initiate bleeding from predisposed sites, such as gastrointestinal ulcers and surgical wounds. However, even in low doses, heparin can affect platelet numbers to a degree that leads to clinically significant bleeding or, paradoxically, thrombosis. Thrombocytopenia associated with heparin can be immune or non-immune related. The non-immune form (heparin-induced thrombocytopenia I [HIT I]) is usually associated with larger doses of heparin and occurs early (within 4 days of use). In contrast, the immune form (HIT II) implies the presence of heparin-dependent antibodies, occurs with variable heparin doses and is more likely than HIT I to result in thrombosis. Up to 3% of patients treated with unfractionated heparin for more than 4 days may develop HIT, but immune-related thrombocytopenia may occur earlier in those who have been previously exposed to heparin and have developed antibodies.<sup>3</sup>

Heparin doses of up to 100 units/kg body weight may be used for full anticoagulation, but, for the maintenance of catheter patency, doses as small as 3 units per hour have been used. Practice has changed, with intermittent flushes several times a day being preferred for peripheral intravenous devices, intermittent flushes perhaps every few days for outpatient central venous lines,<sup>4</sup> and continuous flushing systems now used in ICUs and high-dependency units.

Many studies have investigated peripheral intravenous catheters, particularly in children, with mixed results.<sup>5–7</sup> For 22-gauge catheters, patency was worse when flushed with saline compared with heparinised saline, necessitating more interventions. For larger gauge catheters (16–20-gauge), patency was surprisingly poor whichever flush was used.<sup>8</sup> Another study found no difference between the two types

of flush, but calculated annual cost savings of switching to saline alone at US\$27 594, comprising nursing time and equipment costs.<sup>9</sup>

Similarly, in adult patients with peripheral catheters (18–22-gauge), patency did not differ between heparin or saline flushes, while significant savings of US\$30 000–40 000 per year were calculated if saline-only flushes were used. Needle-stick injuries, which are more likely with heparin locks, would also be reduced with saline-only flushes.<sup>10</sup> Other small and large studies in adults found equal effectiveness for heparinised and normal saline, and for varying heparin concentrations.<sup>11–14</sup> Another study found that 24-hourly saline flushes were as good as heparin flushes (50 units) 8- and 24-hourly. Annual savings in the cost of disposables could have been US\$19 000, and in nursing time could have been 700 hours per year.<sup>15</sup>

A meta-analysis of heparin and saline flushes for peripheral intravenous catheters showed that saline was as effective as heparin, and calculated a potential saving of US\$109 to US\$218 million through use of saline alone. This saving came from the lower cost of saline and reductions in anticoagulant side effects and drug incompatibilities.<sup>16</sup>

For central lines, studies showed that saline flushes were as effective at maintaining patency as heparin solution flushes.<sup>4,17,18</sup> A long-term study (up to 24 months) in cancer patients using 98 Groshong and Port-a-cath catheters found a very low rate of complications, whichever flushing solution was used.<sup>19</sup>

An historical case-control study of arterial lines showed much better performance if 20-gauge rather than 18-gauge catheters were used, while continuous flushing was better than intermittent flushes when observing for thrombus formation with arteriography. Heparin-impregnated catheters also performed worse than Teflon catheters.<sup>20</sup> A similar sized study randomised adult patients with arterial cannulas to receive saline or heparinised saline (2 units/mL) as a continuous flush. Although the study period was limited to 96 hours, there was no difference between the groups for duration of patency or failure rates, but accuracy of blood pressure measurement (when compared with non-invasive blood pressure measurement) was found to be better with heparinised saline.<sup>21</sup> A slightly smaller study comparing hourly flushes of heparinised saline (2.5 units/mL) and saline found no difference in patency or accuracy of pressure measurements. Most patients were studied for only 72 hours. There was more frequent damping of the saline flushed lines, but this was correctable with repositioning and flushing.<sup>22</sup>

In contrast, a small study in medical ICU patients showed a significant improvement in catheter survival (up to 96 hours) and accuracy of blood pressure measurement when

heparinised saline (4 units/mL) was continuously flushed at 3 mL/hour.<sup>23</sup>

A study of the patency of both central and arterial lines with continuous flush systems also showed comparable function between heparinised saline and saline-flushed lines. However, this again was an historically comparative study, which also compared five different flush systems and two types of arterial cannula.<sup>24</sup>

An alternative to heparin is sodium citrate which, as a 1.4% solution, has been compared with heparinised solutions (4 units/mL) as a continuous flush for arterial lines. There was no difference in catheter survival and complication rates between the two groups, but observations continued only up to 96 hours.<sup>25</sup>

A meta-analysis in 1991 of published and unpublished research on the efficacy of heparinised and normal saline solutions in maintaining patency of intravascular lines showed that, for intravenous catheters, there is no significant difference. For intra-arterial lines, there were only two studies (by the same investigator), which was considered too small a sample to draw conclusions.<sup>26</sup>

The results of our study concur with those of many others, and show that heparin as a continuous flush at 3 units/hour does not improve the function of arterial lines compared with continuous flushing with normal saline. The findings of this study could have been enhanced by a larger study group, particularly as this might have reduced the degree of skew of the data, and also by comparing the accuracy of blood pressure measurements.

Our ICU policy has now changed to using normal saline as the preferred flushing solution. We expect no increase in catheter failure rates, and also a reduced likelihood of drug incompatibilities and heparin-associated adverse effects.

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