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Aluminium content of infusion and irrigation fluids

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Severe problems can arise when subjects accumulate aluminium and this becomes serious when it is accompanied by compromised renal function (Ward and Parkinson, 1983). Manifestations of aluminium toxicity include vitamin D-refractory osteodystrophy, hypercalcaemia, anaemia and severe progressive encephalopathy. The problem of aluminium toxicity has been highlighted by the review by D'Arcy (1985) and by two recent clinical studies. In the first of these, Milliner et al. (1985) found that albumin-replacement solutions were a rich source of aluminium. The mean concentration of aluminium in the 59 bottles of human serum albumin (5 different suppliers) tested was 363 μg (13.4 μmol) per litre (range: 64–2570 [2.4–95.3]). Aluminium concentrations were also measured in Ringer's lactate, normal saline, and an acid –citrate–dextrose solution used as an anticoagulant. Aluminium concentrations in these solutions were 7.4, 2.6 and 74 to 103 μg/l, respectively.

The second study by Sedman et al. (1985) examined the possibility that premature infants might be vulnerable to aluminium toxicity acquired through intravenous feeding. The results of their prospective study clearly showed that infants who had been fed intravenously had an aluminium loading that was reflected in increased urinary excretion of aluminium and elevated concentrations of the metal in plasma and bone. Indeed bone aluminium concentrations in infants who were fed intravenously were 10 times higher than those of infants who had received limited intravenous feeding.

Sedman et al. (1985) also tested a range of commonly used intravenous solutions and showed that aluminium contents ranged from (mean $\pm$ S.D.) 6 ± 4 μg/l for sodium chloride solution (4000 mmol/l), to $16{,}598 \pm 1801$ μg/l for potassium phosphate solution (3000 mmol/l). More recently aluminium contamination within the range 1–3430 μg/l has been found in intravenous fluids used in paediatric practice in the U.K. (McGraw et al., 1986).

The question of where the aluminium comes from in these solutions has only partially been answered. Certainly aluminium is present in relatively high concentration in commercial solutions of human albumin, but the primary source is unclear. However, since albumin solutions are obtained from normal human plasma, it would seem that the aluminium must be an artifact of collection, processing or storage. The fact that other infusion fluids also contain aluminium (although generally at a lower concentration than albumin solutions) may well indicate some common factor

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causing the contamination, for example the distilled water used, the containers and closures, or the sterilization procedures.

The aim of the present study was to examine a range of sterile infusion or irrigation fluids prepared locally (commercial or hospital manufacture) in Northern Ireland for their aluminium content, and then attempt to isolate the source of the contaminating metal. The solutions to be examined were chosen to give a range of container types including some with aluminium caps.

Twenty-five fluids were analyzed for aluminium content using a flameless ionization Perkin-Elmer HGA 300 furnace. The detection system was a Perkin-Elmer 4000 atomic absorption spectrophotometer. All samples were analyzed in triplicate. The fluids tested, their source, container type and aluminium content are shown in Table 1.

All the solutions tested had a very low aluminium content ranging from 0.2 to 11.3 μg/l (Table 1). One mean value of 25.0 μg/l was recorded, however, as indicated in the table, this was due to contamination from the aluminium screw cap of the container. Other solutions in

TABLE 1

ALUMINIUM CONTENT OF A RANGE OF STERILE FLUIDS MANUFACTURED IN NORTHERN IRELAND TOGETHER WITH INFORMATION ON CONTAINERS AND CLOSURES

Sterile fluid and manufacturer	Number of samples	Container type	Container closure	Aluminium content (μg/l)
Sodium chloride injection BP 0.9% w/v (500 ml), RVH *	3	glass bottle	crimped aluminium cap; rubber liner	4.7, 5.2, 5.6
Water for injection BP (500 ml), RVH *	3	glass bottle	crimped aluminium cap; rubber liner	9.8, 9.8, 10.2
Sodium chloride 0.9% w/v for irrigation, IVEX *	1	polypropylene bottle	polypropylene hermetically sealed cap	0.6
Sterile water for irrigation IVEX *	2	polypropylene bottle	polypropylene hermetically sealed cap	< 0.2, 0.6
Dextrose 4%, sodium chloride 0.18% w/v, (750 ml); citrate phosphate dextrose BP (50 ml) GRL *	1	PVC bag	–	5.3
Manitol intravenous infusion BP 20% w/v, GRL *	1	PVC bag	–	0.6
Intraneal No. 4, GRL *	1	PVC bag	–	11.4
Sterile water for irrigation GRL *	1	PVC bag	–	< 0.2
Sodium chloride intravenous infusion BP 0.9% w/v, GRL *	2	PVC bag	–	2.1, 5.0
Glucose intravenous infusion BP 5% w/v, GRL *	2	PVC bag	–	3.9, 7.5
Potassium chloride 0.2% w/v and sodium chloride 0.9% w/v intravenous infusion BP, GRL *	2	PVC bag	–	2.2, 3.2
Sodium chloride 0.18% w/v and glucose 4% w/v intravenous infusion BP, GRL *	3	PVC bag	–	5.1, 5.1, 11.3
Stills test (distilled water, sterilised), RVH *	3	glass bottle	aluminium screw cap; rubber liner	1.8, 3.9, 25.0 **

* Manufacturers:
RVH, Sterile Fluids Unit, Royal Victoria Hospital, Belfast, N. Ireland;
IVEX, Ivex, Larne, Co. Antrim, N. Ireland;
GRL, Galen Research Laboratories, Antrim, Co. Antrim, N. Ireland;

** Concentration of aluminium increased during each of 3 measurements; contamination presumably arising from aluminium screw cap which was removed each time prior to sampling.

containers with aluminium caps had lower aluminium concentrations, thus the possibility of the aluminium caps being a common source of contamination is unlikely. Also since the solutions in different types of containers (e.g. glass bottle, PVC bag, polypropylene bottle) had similar (and low) aluminium concentrations, it seems unlikely that there is a common source of contamination in the containers. Furthermore distilled water collected from distillation plants and sterilized also had a low aluminium content suggesting that such stills were not a source of contamination.

Previous studies have suggested that aluminium contamination is particularly high in solutions containing calcium and phosphate salts, heparin, and human albumin (Milliner et al., 1985; Sedman et al., 1985). It is interesting to note in this respect that Loeliger and de Wolff (1985) have identified a possible source of the aluminium contamination of albumin solutions, namely the aluminium hydroxide gel used to absorb vitamin K-dependent coagulation factors prior to the separation of various fractions for clinical use. Since aluminium is strongly bound to albumin, it may remain as a contaminant of commercially available albumin products.

However, the source of aluminium in other intravenous solutions is still not established. The present work tends to exonerate containers and closures (with the sole exception of the aluminium screw cap), and water taken directly from the still and sterilized. The purity of the materials used in the manufacture of infusion solutions, and possibly any storage of distilled water prior to usage, are other factors which at present cannot be excluded as sources of aluminium contamination. The subjection of water and ingredients to special testing for aluminium content prior to use in formulations would seem to be mandatory.

Until the problem is resolved, the aluminium status of patients receiving prolonged intravenous infusion therapy should be reviewed regularly. Premature infants fed intravenously and adult patients with impaired renal function would seem to be at particular risk from aluminium contamination.

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