

AN ASSESSMENT OF IV ANTIBIOTIC RECONSTITUTION METHODS

By DANIELLE TURNER, BPHARM, MRPHARMS, ALISON EGGLETON, MSc, MRPHARMS, and BRIT CADMAN, BPHARMS, MRPHARMS

- **OBJECTIVE** — *To investigate the feasibility of replacing a standard method of intravenous antibiotic reconstitution.*
- **DESIGN** — *An on-ward comparison of the standard method with two novel reconstitution methods, the Baxter Minibag Plus (MBP) and the Macoflex Transfer Set (MTS) drug reconstitution system.*
- **SETTING**: *Two general surgical wards at Addenbrooke's Hospital, Cambridge.*
- **MAIN OUTCOME MEASURES** — *Reduction in reconstitution time, errors and interruptions, and improvement in patient and staff safety.*
- **RESULTS** — *Time savings of over 4.5min per reconstitution were observed with both the MBP and MTS. Problems were experienced with 80%, 60% and 20% of reconstitutions for the standard method, MBP and MTS, respectively. The average number of interruptions were significantly reduced with the MBP and MTS systems. 61% of respondents for the MBP and 88% for the MTS found the product easier to use than the standard method. Over 82% of respondents agreed that the MTS offered the advantages of rapid preparation, easy preparation, no needle-stick injuries, reduced risk of contamination and reduced handling. With the MBP, 61% of respondents experienced difficulty in connecting it and 83% experienced air in the infusion line, compared with 12% of each, respectively, for the MTS. 61% of respondents supported the possible introduction of the MBP over the standard method, while 94% supported the possible introduction of the MTS to Addenbrooke's Hospital. The cost saving per dose using the MBP was 17p and 96p using the MTS.*
- **CONCLUSION**: *The introduction of the MTS to Addenbrooke's Hospital as an intravenous antibiotic reconstitution method was recommended.*

Many hospitals, including Addenbrooke's Hospital, do not have the facilities to provide a full centralised intravenous additive service (CIVAS). This results in a significant amount of drug reconstitution being carried out by nurses on the wards. However, these conditions are less than ideal for IV drug preparation, with pressure on time and interruptions during the reconstitution process increasing the risk of bacteriological contamination and drug errors. In an attempt to address these issues a number of companies have launched novel reconstitution systems with the aims of increasing safety for both nurses and patients, reducing the risk of drug error, minimising contamination and reducing preparation time.

Ideally, hospital pharmacies should be seeking to provide wards with IV drugs in a reconstituted form. This would then avoid the necessity of performing reconstitutions in hospital wards under non-aseptic conditions by ward-based staff, such as nurses and junior doctors,¹ and would be in line with recommendations in the 1976 Breckenridge Report.² The report stated that "the necessity to add drugs to sterile intravenous fluids on the ward should be reduced to a minimum" and that "the addition of drugs to intravenous fluids in an aseptic pharmaceutical procedure should ideally be carried out in appropriate conditions under the direct control of a pharmacist". However, the high initial capital required and the competing demands it would place on pharmacists' time, mean that such a service will be unavailable in Addenbrooke's Hospital for the immediate future.

The current reconstitution method of antibiotics on the wards involves reconstitution of the dry powder with an appropriate diluent, using a needle and syringe. Dilution, by adding the reconstituted antibiotic to an infusion bag via the latex injection port, is necessary for some antibiotics. This procedure has a number of disadvantages, including the risk of microbiological or particulate contamination of the dose as a result of poor aseptic technique, which can result

in septicaemia or phlebitis and hazards to nursing and medical staff.³⁻⁷ Frequent interruptions during preparation, cramped preparation areas and a lack of time have also been postulated to result in errors, including incorrect selection of drug or diluent, preparation of an incorrect dose and the incorrect method or rate of administration.^{3,8-10} The risk of aerosolised antibiotic, which can result in the repeated exposure of staff to these drugs and a possible increase in antibiotic resistance, as well as the risk of needle-stick injury, are also commonly associated with this method of preparation.¹¹ It should, however, be noted that this method of reconstitution enables multiple and part doses to be added to one bag, when required.

The purpose of this study was to analyse whether a novel reconstitution method could offer advantages over the standard practice of needle and syringe reconstitution. The Macoflex Transfer Set Drug Reconstitution System (MTS) from Maco Pharma Ltd and the Flagyl Minibag Plus (MBP) from Baxter Healthcare Ltd were compared with the standard method for ward preparation of cefotaxime/metronidazole mixtures and an on-ward assessment of the use of these methods conducted. The cefotaxime/metronidazole combination was chosen for study because it is the antibiotic prophylaxis regimen most widely prescribed on the surgical wards and therefore a high exposure of staff to the use of a new product was expected. If successful, the intention was then to encourage nurses to use the system for other antibiotic reconstitutions (which would involve using 0.9 per cent w/v sodium chloride or 5 per cent w/v glucose — both of which were available in the novel systems).

The benefits of the MBP and its usage have been described in detail previously,^{12,13} although they are mentioned briefly again here. The MBP requires the user to attach a vial to a port on the infusion bag and to reconstitute the powder using the fluid from the bag. The vial then remains attached throughout the infusion and only one dose may be added to an infusion bag.

The MTS comprises a Maco Pharma minibag with an additive port that incorporates a double membrane. The double membrane surrounds an inner sterile chamber that enables a closed system to be

At the time this work was carried out Danielle Turner was a preregistration trainee, Alison Eggleton was principal pharmacist for education and training and Brit Cadman was principal pharmacist for clinical services at Addenbrooke's Hospital, Cambridge

maintained during reconstitution. A single use transfer device, with a needle shielded at both ends is used to puncture the first membrane of the additive port while keeping the second membrane intact. The transfer device with the vial attached is then pushed through the second membrane. Again, the fluid from the infusion bag is used to reconstitute the powdered antibiotic, although in this case the transfer set may be withdrawn from the first membrane, while still remaining attached to the infusion bag, and multiple vials attached enabling more than one dose to be administered with one infusion bag.

It has been suggested that an advantage of the MBP is that it does not require an additive label, because the vial remains attached to the infusion bag throughout administration.¹² However, IV drug administration policy at Addenbrooke's Hospital requires a label, giving the drug added and the time of reconstitution, and signed by two trained staff, to be attached to every intravenous infusion in order to maximise patient safety. Our staff were therefore still required to attach a label to the MBP. In addition, a recent paper evaluating the use of the MBP system reported that a number of respondents had felt that the absence of an additive label could increase the chances of an infusion not being checked and of the time of preparation not being noted.¹²

An examination of the on-ward use of these two products was conducted and compared with the current method of antibiotic reconstitution.

METHODS

Two novel methods were introduced to the two participating surgical wards for four weeks each. The MBP was introduced first, and then the MTS. Before the start of the two trials, the nurses were observed using the current standard method and the same measurements were taken for the standard method as for the novel methods.

To ensure uniformity of training, all participating staff nurses attended two training sessions (one for the MBP and one for the MTS) conducted on both wards immediately before the relevant product's launch. Training in the use of both methods was carried out by the same member of the pharmacy department, according to instructions previously received from the company representatives.

Staff had the usual access to the medicines information line in the pharmacy department in case of difficulties but otherwise received no other support in the use of the novel systems. Staff were encouraged to use the new systems for all cefotaxime/metronidazole administrations and they were not warned as to when a member of pharmacy might be present on the ward to monitor the administrations. No readings were taken in

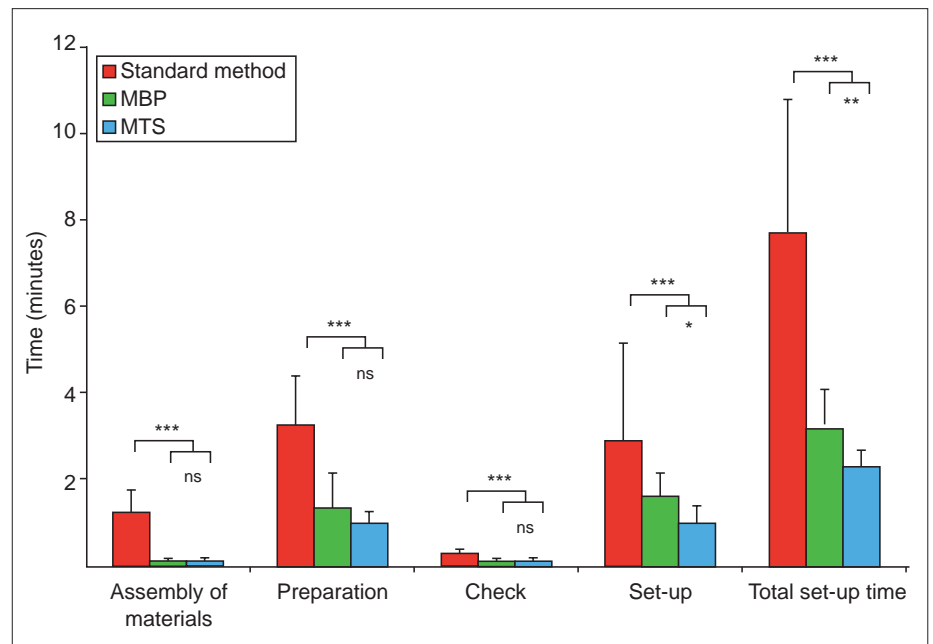


Figure 1: Comparison of the times taken for each stage of preparation for the standard method, MBP and MTS (n=10 for each method, *** P<0.001, **P<0.01, *P<0.05, ns=not significant)

the first week after introduction of each new method, in order to enable the staff to become familiar with the system.

The time taken to reconstitute 10 doses of cefotaxime and metronidazole using each method was recorded by observing the trained nursing staff on the ward. Different staff were observed at random times during the 2pm drug round from an unobtrusive distance and no assistance or advice was given during the observation period. Data were collected on a standard form and timings were recorded separately for each step of the process using a stop watch. The same person conducted all readings in order to minimise variability in the results.

The following stages of the preparation process were timed as follows:

- Time taken to assemble all the materials necessary for the reconstitution, including writing the label
- Time required to prepare the infusion bag (as measured from the time all materials were assembled until another member of the nursing staff was called for the double-check)
- Time taken to perform an appropriate checking procedure (double-check)
- Time taken to connect the line to the patient (set up)

The number of interruptions was also noted by the observer, although the duration of the interruptions was not included in the reconstitution times. If any problems were identified, these were recorded although no assistance was given.

In brief, to investigate the effect of the two systems in comparison with the standard method, differences between group mean were analysed using a one-way analysis of

variance (three levels). To clarify the nature of any identified differences, planned orthogonal contrasts comparing the two novel methods and the effects of each one in comparison with the standard method were performed where appropriate.

On completion of each four-week trial, all the nurses involved in intravenous administration were given questionnaires to complete (anonymously) regarding their opinion of the novel methods in comparison with the standard method.

The total cost of the materials involved in each method of reconstitution was calculated according to the current list prices at the time of the study. Items included in each calculation were as follows:

Standard method Metronidazole 500mg Braun bag (100ml), cefotaxime 1g vial, needle, 5ml syringe, water for injections 5ml ampoule

MBP method Metronidazole 500mg MBP bag (100ml), cefotaxime 1g vial

MTS method Metronidazole 500mg MTS bag (100ml), cefotaxime 1g vial, Macoflex transfer set

RESULTS

The results of the timings described in the methods section are shown graphically in Figure 1. Nurses administering the reconstituted antibiotics required significantly less time with both the novel methods compared with the standard method (F[2,29]=24.60, P<0.001), with a total average saving of over 4.5 minutes being observed with both novel methods. In addition, the MTS was significantly faster than

Table 1: Nurses' responses on the ease of use of the novel systems

	Nurses agreeing with statement (%)		
	MBP vs standard	MTS vs standard	MTS vs MBP
Much harder	17	0	0
A little harder	17	6	0
No difference	5	6	12
A little easier	44	24	35
Much easier	17	64	53

Table 2: Nurses' agreement with presented advantages of the MTS system

Advantage	Nurses agreeing (%)
Rapid penetration	82
Easy preparation	94
No needle stick injury	82
Minimal contamination	82
No aerosol formation	71
Protects staff	76
Less handling involved	88
Device usable for other reconstitutions	88

the MBP ($F[1,19]=8.192, P=0.010$). This difference was attributable to a significant saving in time in the set-up stage with the MTS compared with the MBP ($F[1,19]=7.919, P=0.011$). There were no statistically significant differences between the two novel methods at any of the other earlier stages ($F[1,19]<0.91, P>0.19$).

In addition, there was a significant reduction in the number of interruptions observed with the novel methods compared with the standard method ($F[2,29]=10.54, P<0.001$). Only 20 per cent of reconstitutions with the MBP and MTS system experienced at least one interruption, while 90 per cent of administrations with the standard method were interrupted at least once by another member of the ward staff. Furthermore, at least one problem was identified with 80 per cent of the administrations using the standard method, 40 per cent using the MBP and 20 per cent using the MTS. This represents a significant reduction in interruptions with the novel methods compared with the standard method ($F[2,29]=4.50, P=0.021$). The most commonly observed problem was air occurring in the line. On completion of the administration, air fell below the drip chamber and entered the infusion line in 60 per cent of the cases with the standard method, 40 per cent with the MBP and 20 per cent with the MTS.

As mentioned, trained staff at the end of each trial completed two questionnaires regarding the use of the MBP and MTS.

Completed questionnaires were obtained from the nurses involved in the trial at the time (18 and 17 nurses for the MBP and MTS trials, respectively). The responses to the questions regarding ease of the use of the two novel systems are shown in Table 1. In addition, as the MTS system was introduced after the MBP, nurses were also asked to state how they rated the MTS system in comparison with the MBP method. As can be seen from Table 1, 64 per cent of nurses said the MTS was much easier to use than the current method, while 17 per cent said the MBP was much easier to use than the current method. In addition, 53 per cent of nurses favoured the introduction of the MTS rather than the MBP. This was most likely due to the fact that 12 of the 18 respondents for the MBP reported experiencing problems with connecting the new system together. Only three nurses believed these problems could be overcome with better training; the others believed the problem was inherent within the design of the MBP, which requires a large amount of force to connect the system together.

The preference for the MTS system was further clarified, with most respondents agreeing with the advantages listed in the questionnaire (and shown in Table 2).

In both questionnaires nurses were asked whether they would like to see the introduction of the novel system they were using to the hospital. The results for the MBP and MTS are compared in Table 3. As can be seen, 28 per cent of nurses said they would definitely support a decision to introduce the MBP and 17 per cent said they were definitely against the introduction of the MBP. This is in contrast to the MTS, where 53 per cent of nurses said they would definitely support the introduction of the MTS and no nurses were against the suggestion.

Using information obtained from the pharmacy purchasing department it was shown that, before this study, the total annual use of 1g cefotaxime on both wards from April 1999 to March 2000 was 5,429 units. During this same period the total annual use of the metronidazole 100ml infusion bag was 6,788 units. Unfortunately, owing to trust confidentiality issues regarding contract prices, the cost of the individual components cannot be quoted. However, the MBP was 17p less costly per dose than

Table 3: Nurses supporting introduction of new reconstitution system

Advantage (%)	Nurses' response (%)	
	MBP	MTS
Definitely not	17	0
Not really	11	0
No preference	11	6
Possibly	33	41
Definitely yes	28	53

the standard method of reconstitution. The MTS offered a cost saving of 96p per dose. Assuming that every single cefotaxime dose was administered with metronidazole and that an equal number of doses were administered on each ward, the potential annual maximum cost saving achieved by each ward would have been approximately £460 for the MBP and £2,600 for the MTS at these prices. The extent to which the devices are used for other reconstitutions (including administrations using 0.9 per cent w/v sodium chloride or 5 per cent w/v glucose as the vehicle) could further enhance these savings. These would be maximal for the MTS device, where (unlike with the MBP system where the adaptor is part of every infusion bag) the MTS transfer set is separate and thus can be used only when required. An additional advantage with the MTS is that the absolute cost of the MTS double-membrane bags and the standard bags stocked by the hospital are the same, eliminating the need to stock a variety of bags for different types of administrations. In addition, the saving of 30 per cent of nursing time seen with both the novel methods may have potential financial benefits, although, since these calculations were merely intended as a guide, this has not been included.

DISCUSSION

This study highlighted a number of issues arising from the standard method of intravenous antibiotic reconstitution. The most prominent, as noted from the observations, was the considerable amount of time taken for the entire process of reconstitution and attachment to the patient, in contrast to the other two methods (Figure 1, p128). The standard method also suffered from a significantly greater number of interruptions, most likely due to the extended preparation time. This has the potential to increase the number of errors made because of distraction and hence any method that decreases this parameter could have significant risk management value.³ The standard method was also the only method where aerosol formation was observed, which poses a risk of repeated exposure of staff to the antibiotic

drugs and increases the likelihood of bacteriological resistance.¹¹ In addition, despite no needle-stick injuries being observed during the trial, the results from the questionnaire suggested that these are a major safety concern to nurses with the standard method of reconstitution.

Of the administrations observed using the MBP, the most noticeable advantage of this product was the considerable time saving when compared with the standard method. A rough estimate of the significance of a saving of approximately 4.5 minutes per reconstitution can be calculated. Each ward involved in the trial has on average four or five patients receiving cefotaxime and metronidazole infusions three times a day (this fluctuates greatly depending on the surgery being performed). This equates to a saving of approximately one hour of nursing time each day per ward. Use of the MBP was also accompanied by a significant decrease in the number of interruptions per dose prepared.

However, in practice, two problems were identified with the use of the MBP, which concerned patient safety and the ease of use by staff. Air fell below the drip chamber and entered the line after the administration of the infusion fluid in 60 per cent of the observed administrations, a problem most commonly resolved by disconnecting the line from the patient and rebleeding it before the next administration. Over 80 per cent of users also stated they had experienced air in the line with the MBP in their questionnaire responses. The observation of air in the line represents a reduction in comparison with the standard method. However, it was still believed an occurrence of 60 per cent was an unacceptable problem to the nursing staff. The second problem was the difficulty of connecting the system together, which was experienced by more than 60 per cent of respondents. This has several implications. One is the risk of possible injury to nurses' wrists and shoulders due to the force required to connect the vial. Of more concern is that infusion bags can be connected to patients with the vial being only partially attached (this was observed on several occasions during the first week of the trial of the MBP) which in turn could result in a significant increase in the risk to the patient of bacteriological contamination. An inquiry into this problem established that it is due to the unavoidable, minor variability in vial top size between manufacturers, which is normally unnoticed. It does, however, become a problem when the vial top size is crucial — such as where a tight fit is required in order to ensure the vial is retained by the MBP port.

In contrast, the MTS offered some benefits over the other two methods. The greatest time saving per dose administered was seen with the MTS (Figure 1). There were also considerably fewer problems

observed with this method, with no problems being observed with 80 per cent of administrations. In addition, which is particularly important, the MTS was the most favoured system. There was confidence and acceptance among the users, with 94 per cent of users in favour of its introduction to the trust. Over 70 per cent of respondents agreed that the MTS offered the advantages of rapid and easy preparation, no needle stick injuries, minimal contamination, no aerosol formation, staff protection, less handling of the product and more flexibility with regard to the number of reconstitutions possible.

Neither of the two novel systems permit the administration of part doses of the powdered antibiotic. However, owing to the similarity of the Macopharma double-membrane bags to the standard single-membrane bags, they are still suitable for use with the standard reconstitution method (when the need arises), unlike the MBP bags which can only be used for whole vial doses. All Macopharma 50ml and 100ml minibags have a double membrane thus enabling use with or without the transfer set. This simplifies staff training and purchasing procedures. Additionally, maximal financial savings were identified with the MTS system.

In conclusion, this study found that both novel systems tested were shown to offer substantial advantages over the current standard method of intravenous antibiotic reconstitution. They both demonstrated considerable time saving and interruption reduction. They also both minimised the risk of needle-stick injuries, exposure to antibiotic aerosol and, with less handling involved, the risk of contamination, thus offering advantages to both staff and patients.

When comparing the two novel methods, it was considered that the MTS presented a more viable option for intravenous antibiotic reconstitution, both in terms of risk management and user acceptability. This was mainly due to significantly fewer problems being experienced with the MTS. The MTS method also offered a decrease in sharps material due to the transfer set (with the needle) being detachable from the infusion bag and thus not requiring simultaneous disposal with the bag, and the highest potential cost saving per dose of intravenous antibiotic administered. Additionally, the potential for unjustifiable increases in the cost of metronidazole usage, if the MBP system was used without a reconstituted antibiotic, and the wastage due to faulty connection of the MBP system, were taken into account when choosing the MTS over the MBP.

Based on the results of this trial and from the opinions gathered, the MTS was introduced to Addenbrooke's Hospital to replace the current standard intravenous drug reconstitution method for metronidazole, normal saline and glucose.

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