



# The effects of mixing different insulin analogues

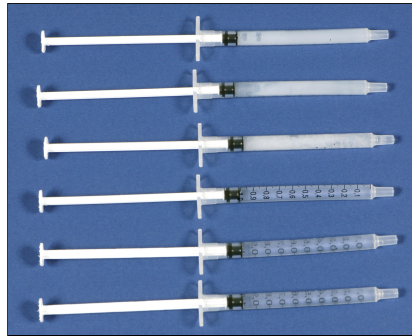
Frequently doctors, specialist nurses and patients are unaware of the interaction between different insulins. We reviewed a needle phobic patient using a subcutaneous cannula device. The patient was using insulin glargine (Lantus) and insulin aspart (Novorapid). He had been advised to use two separate devices to keep the insulins apart. However, he was using the one device to give both insulin types and had experienced no problems.

Unlike most other insulins which are soluble at a neutral pH, insulin glargine is soluble at a pH of 4. The slightly acidic nature of glargine is the reason it can sting when injected. The manufacturer (Sanofi-Aventis) advises that it is never diluted or mixed with other insulins and that it should only be used if it is clear and colourless with no particles visible.

We demonstrate the effects of mixing insulin glargine with short acting insulin analogues. In each of six 1ml syringes we mixed 50 units of a long acting insulin analogue, either glargine (Lantus) or detemir (Levemir), with 50 units of a short acting analogue: aspart (Novorapid), lispro (Humalog) or glulisine (Apidra).

All of the short acting insulins mixed with insulin glargine immediately formed a cloudy white precipitate which gradually settled at the bottom of the syringe. In contrast, no precipitate was seen with the same short acting analogues mixed with detemir (see Figure 1).

Adding an insulin with a slightly acidic pH on to an insulin with a neutral pH results in a solution with



**Figure 1.** From top to bottom: (1) Lantus + Novorapid; (2) Lantus + Humalog; (3) Lantus + Apidra; (4) Levemir + Novorapid; (5) Levemir + Humalog; (6) Levemir + Apidra

a pH part-way between the two (depending on the proportions of the two insulins). At the new pH, neither insulin will now be soluble. The insulin molecules form crystals which precipitate out of solution. This reduces the effectiveness of the insulin dose.

Subcutaneous cannulae can be useful devices where patients might otherwise omit insulin doses because of needle phobia. Available brands include the Insuflon (Applied Medical Technology Ltd, Cambridge, UK) and the i-port (Patton Medical Devices, Austin, Texas, USA). These can be used for insulin but also for other repeated subcutaneous injections such as growth hormone, heparin, analgesics or G-CSF.

These injection ports reduce pain and anxiety around repeated injections.<sup>1</sup> Studies in children show that their use can improve glycaemic control. In one study, HbA<sub>1c</sub> dropped from 9.4% (79mmol/mol) to 8.5% (69mmol/mol) over six months.<sup>2</sup> They are designed to be changed every three to five days.

They are not available on prescription on the National Health Service but patients can purchase them. They are not widely used, either because of the cost or because doctors and specialist nurses are unfamiliar with them.

We demonstrate why patients should be advised to use a separate injection port for the two different insulin types, especially if the long acting insulin is glargine. This advice is also relevant to patients injecting the two insulins with insulin pens. The two injections should be performed in two separate sites as precipitation of insulin crystals can occur within the subcutaneous layer.

We hope that by publishing this we enlighten many more doctors and specialist nurses to ensure their patients are keeping the Lantus injection site rotation away from the short acting insulin injection site rotation.

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## Declaration of interests

There are no conflicts of interest declared.

## References

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