Posology of insulins: A review of standard textbooks and product inserts

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ABSTRACT

Objectives: The study is aimed to assess whether the information contained in standard pharmacology, endocrinology, and diabetology textbooks regarding timings of administration, frequency and dose of various insulins is adequate and also to see whether the information contained in these texts is concordant with product inserts. Materials and Methods: Four standard textbooks of pharmacology, two of diabetology and three of endocrinology were assessed for the published information regarding dose, timing, and frequency of insulin administration. The product inserts of commonly available insulins in India were also studied for the same. Results: Various omissions and disparities could be seen in the coverage of insulins in standard textbooks. Posology information about premixed insulins and basal insulins have been omitted by the majority of the textbooks. Details about dose, frequency and timings of ultra-short acting insulins have also not been covered by all textbooks. Some discrepancies regarding prescribing information was also noted in product inserts, especially in case of newer insulins. Conclusions: Thus, this article stresses upon the need of a uniform source of information for providing adequate and standardized knowledge regarding timing, frequency, and dose of insulins.

Key words: Insulins, patient information leaflet, posology, product insert

INTRODUCTION

Insulin therapy is often an important part of diabetes treatment. The purpose of giving insulin in diabetes mellitus is to restore metabolism to normal, avoid symptoms due to hyperglycemia and glucosuria and to prevent short-term and long-term sequelae of diabetes. In order to reach these goals and to avoid potentially dangerous side-effects like hypoglycemia, it is vital to administering insulin in appropriate dose and frequency and at correct timings. This is possible only with accurate knowledge about the posology of various commercially available insulin preparations.

Materials and Methods

Some of the most popular and most commonly read textbooks of pharmacology, diabetology, and endocrinology, are an important and reliable source of such information, both for students and clinicians. This article aims at assessing the adequacy of the knowledge provided by these textbooks regarding posology that is, dose, frequency, and timing of insulins. Apart from textbooks, package inserts, and patient information leaflets also play an important role in spreading knowledge and awareness, especially among patients. In this article, we would also focus on assessing the information contained in the package inserts and see if this information is concordant with the information given in the textbooks.

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Table 1: Comparison of information about insulins in pharmacology, diabetology and endocrinology textbooks

| Drug class            | Drug                  | Goodman and Gilman’s The pharmaceutical basis of therapeutics[1] | Basic and clinical pharmacology[2] | Essentials of medical pharmacology[3] | Principles of pharmacology[4] | Endocrinology[5] | Text book of diabetes[6] | Text book of diabetes mellitus[7] | Manual of clinical endocrinology[8] | Williams Textbook of Endocrinology[9] |
|-----------------------|-----------------------|------------------------------------------------------------------|------------------------------------|--------------------------------------|-----------------------------|-----------------|--------------------------|-----------------------------|-------------------------------------|-------------------------------------|
| Ultra short acting insulins | Aspart               | ≤ 15 min before a meal                                            | Immediately before the meal        | Not mentioned                       | Used with long acting insulins | Up to 15 min before meals or immediately after meals | Not mentioned                      | 10–15 min prior to meals | 15 min before to min after meals | Immediately before or after meals |
| Lispro                | ≤ 15 min before a meal | Immediately before the meal                                       | Not mentioned                       | Used with long acting insulins       | Not mentioned                      | Not mentioned      | Not mentioned      | Not mentioned                      | Not mentioned                      | Not mentioned                      |
| Glulisine             | ≤ 15 min before a meal | Immediate before the meal                                         | Not mentioned                       | Used with long acting insulins       | Not mentioned                      | Not mentioned      | Not mentioned      | Not mentioned                      | Not mentioned                      | Not mentioned                      |
| Short acting insulin  | Regular human insulin | 30–45 min before a meal                                            | 30–45 min subcutaneous injection,½–1 h before meal | Not mentioned                       | Not mentioned                      | 30–60 min before meals | 30 min or even longer before meals | 30 min before meals | 30 min before meals | 30–60 min before meals |
| Basal insulins        | NPH (isophane)        | Once a day (at bed time) or twice a day (with short acting insulins) | Mostly combined with regular insulin (70:30 or 50:50) and injected subcutaneous, twice daily (before breakfast and before dinner) | Not mentioned                       | Not mentioned                      | Not mentioned      | Not mentioned      | Not mentioned                      | Not mentioned                      | Not mentioned                      |
| Glargine              | May be administered any time during the day. Sometimes splitting of dose required (prebreakfast and presupper) | Once or twice (split dosing) a day                                 | Once daily injection mostly injected at bed time but may also be given before breakfast subcutaneous injection, twice daily administration | Not mentioned                       | Not mentioned                      | Not mentioned      | Not mentioned      | Not mentioned                      | Independent of meal time            | Usually before bedtime             |
| Detemir               | Twice daily administration | Given twice a day                                                  | Not mentioned                       | Not mentioned                       | Not mentioned                      | Not mentioned      | Not mentioned      | Not mentioned                      | Independent of meal time            | Usually before bedtime             |
| Degludec              | Not mentioned         | Not mentioned                                                     | Not mentioned                       | Not mentioned                       | Not mentioned                      | Not mentioned      | Not mentioned      | Not mentioned                      | Once in 24 h with variable timings | Not mentioned                      |
| Insulin combinations  | Protamine lispro (NPL) and lispro (75/25 and 50/50 ratio) | Not mentioned                                                     | Not mentioned                       | Not mentioned                       | Not mentioned                      | Not mentioned      | Not mentioned      | Not mentioned                      | Not mentioned                      | Not mentioned                      |
|                       | Protamine aspart (NPA) and aspart (70/30 ratio) | Not mentioned                                                     | Not mentioned                       | Not mentioned                       | Not mentioned                      | Not mentioned      | Not mentioned      | Not mentioned                      | Not mentioned                      | Not mentioned                      |

Contd...
were included in this study. Four standard textbooks of pharmacology (2 by Indian authors and 2 by US authors) were analyzed. Two textbooks of diabetology were also studied of which 1 textbook is by Indian author and other is by US author. Three textbooks of endocrinology (2 US and 1 Indian in origin) were also assessed for the desired information. Apart from this, information contained in the package inserts of some of the common commercially available drugs in India was also studied.

**RESULTS**

The results of the analysis are tabulated in Tables 1 and 2. Table 1 shows the comparison of information about insulins available in different textbooks. Table 2 shows information available on the package inserts of some of the most commonly used insulins in India.

**DISCUSSION**

Insulin is a molecule which is now available in multiple formulations and analogs. Almost all text books cover insulin extensively, but information regarding timing of the injection is often discordant. While most authors suggest injecting insulin aspart, lispro or glulisine ≤ 15 min before a meal, others advise immediately preprandial, and postprandial dosage. The recommendations for regular human insulin are uniform in 8 books. Virtually no book mentions premixed insulin analogs and their method of administration. This may be due to the fact that premixed insulins are not frequently used in the US. It must be mentioned, here, however, that premixed insulins are the most commonly prescribed injectable therapy for diabetes in India. It is expected, therefore that Indian books cover this aspect of insulin pharmacotherapy adequately.

Basal insulin analogs are covered by five books while neutral protamine Hagedorn (NPH) insulin is mentioned only by three. The pharmacology books offer varied advice for the dosage of NPH. The novel insulin degludec is covered in current editions of Indian endocrinology and diabetology texts.

The newer insulins analogs present a challenge for the clinical diabetologist. While it is assumed that all analogs share the same prescribing information the product inserts reveal otherwise. Product insert guidelines [Table 2] should be followed while advising the use of all insulins.

**CONCLUSION**

This study stresses upon the need to have standardized, uniform sources of information regarding posology of
insulins. Such information is vital for the better education of students and clinicians, which in turn would ensure the better health care of the patients.

Limitations
The missing information as highlighted in the results and discussion may be available in the new upcoming editions of the textbooks. Only the more commonly used textbooks of pharmacology, diabetology and endocrinology were analyzed for the purpose of this study.

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