Subcutaneous Administration

Evolution, challenges, and the role of hyaluronidase

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BACKGROUND: The subcutaneous (SC) route has evolved significantly. More than two dozen chemotherapy and supportive therapies have been approved for use in the oncology setting. Several IV therapies have been approved for the SC route and require a significantly higher volume than historical maximum limits. Differences exist in how these drugs are administered as compared to older chemotherapy agents.

OBJECTIVES: The purpose of this article is to provide a brief history of the SC route and describe its role in cancer treatment. The use of recombinant hyaluronidase is reviewed within the context of SC monoclonal antibodies. Proper administration techniques and interventions for reducing patient discomfort are discussed.

METHODS: Sentinel medical texts, pharmacokinetic studies, manufacturer's recommendations, and peer-reviewed articles were examined.

FINDINGS: The SC route offers several advantages over the oral and IV routes. A clear understanding of anatomical site selection and injection techniques is beneficial for providing requisite patient education.

KEYWORDS
subcutaneous route; hyaluronidase; monoclonal antibodies; administration

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THE NUMBER OF CHEMOTHERAPY AND BIOTHERAPY AGENTS that can be administered by the subcutaneous (SC) route lags far behind those given orally and via IV (U.S. Food and Drug Administration, n.d.). Between 1969 and 2012, only 11 SC drugs were approved for cancer treatment. However, as other aspects of cancer treatment have evolved over time, so too has the SC route of administration. The approval of high-volume SC monoclonal antibodies (mAbs) has challenged some long-established rules on administration, and valuable new information on injection techniques and pain minimization for all injections has emerged (Locke et al., 2019; U.S. Food and Drug Administration, 2021).

Methods

A literature search, using CINAHL®, Google Scholar, Ovid, and PubMed®, was performed between November 2020 and March 2021. Search terms included *syringe*, *hypodermic*, *needle*, *injection*, *subcutaneous*, *chemotherapy*, *insulin*, *heparin*, *chemotherapy*, and *morphine*. To obtain historical information, medical texts from the 19th and 20th centuries were also included.

Evolution of the Subcutaneous Route

Primitive syringes date back to the Roman Empire where they were used for performing enemas (Friedenwald & Morrison, 1940; Milne, 1907). By the 18th century, physicians were experimenting with methods of introducing medication into SC tissues. Unsuccessful techniques included coating the tip of a lancet with a drug and placing it under the skin, and chemically abrading the skin prior to applying a poultice or balm (Mogey, 1953). In 1713, French surgeon Dominique Anel developed a miniaturized metal syringe with a tapered lancet for aspirating lacrimal ducts (Price, 1969). However, it took more than 130 years before the precursor to the modern needle was invented by Frances Rynd. Rather than using a syringe, Rynd attached his needle to a modified surgical trocar and used gravity to drip morphine into SC tissue (Zakon, 1953). The technique was effective but cumbersome to execute. To improve this method, Scottish physician Alexander Wood crafted a glass version of the Anel syringe and attached Rynd's needle. In 1853, he successfully treated several patients with morphine and called his new route of medication administration "subcutaneous" (Mogey, 1953).