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Spinal Opiate Analgesia

Experimental and Clinical Studies

Edited by
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Preface

The recent development of the use of spinal opiates as a rational therapy for pain rests on clear and certain experimental data. We have long known the spinal cord to be a highly complex structure. Anatomical studies of the substantia gelatinosa have repeatedly demonstrated signs of massive synaptic interaction between primary afferents, descending pathways and intrinsic neurons. Yet, to date that knowledge, insofar as clinical therapy is concerned, has permitted us only to destroy certain connections within the spinal cord in the hopes that the substrate mediating pain could be anatomically differentiated from those which mediate other function. Though cordotomies are clearly effective under certain circumstances, they suffer from the fact the spinal cord is not organized in such an anatomically discrete fashion as is often times drawn in basic medical text. Rather, functions intertwine exquisitely and specific physical interventions are no more likely to produce a specific effect than smashing of the fingertip with a hammer will produce just a loss of the fingernail. The development of specific therapies of the spinal cord has come about by our growing awareness of the intricate organization of the pharmacological substrates associated with specific neural function. Thus, ten years ago had someone suggested the possibility of controlling pain transmission by specifically blocking a pain transmitter, the suggestion would have been foresightful, but groundless, as we had no concept of the fact that there might be different primary afferent transmitters for the different sensations. Though we are still not aware of such specific separations, the observation that primary afferents may contain one of several peptides including substance P, vasoactive intestinal peptide and cholecystokinin, leads us to suspect that these afferents may subserve different functions.

Similarly, we have become increasingly aware of the practical significance of the early literature which indicated that the spinal cord was under massive control by intrinsic and extrinsic modulatory systems. We are now aware, that such modulatory systems are likely associated with the release of a number of specific neurotransmitters, including monoamines, certain amino acids, and most definitely, intrinsic opioid-like materials. It is classical knowledge

that opiates exert a local effect on spinal function. It is only a small step therefore to ask the question of what function these pharmacologically defined modulatory systems have on the behavior of intact and unanesthetized organisms. We can do this by intrathecally administering the putative agonist in an effort to activate the receptors with which those modulatory systems are associated. The affirmative results of this line of investigation make it but a small step to seek similar information regarding the relevance of such effects in the clinical model.

Thus, the present volume is part of the "Zeitgeist" that represents a growing awareness of the use of such specific modulatory substrates in the spinal cord to modulate the rostrad processing of behaviorally relevant somatic and visceral information. The present volume is a selection of the presentations which were made at the first international sessions dealing with the use of spinal opiates for analgesia in chronic pain and perioperative analgesia. Least one think that this trend is of minor consequence, he need only consider the fact that this volume presents the results of over 2000 cases where epidural or intrathecal opiates were applied for the relief of chronic pain associated with a variety of afflictions including cancer. Moreover, as reflected in these papers, an important use of spinal opiates may well be in their ability to minimize not only the pain suffered by postoperative patients, but also the autonomic sequelia which result from surgical invasion under otherwise adequate surgical anesthesia.

As editors, we have attempted to maintain a standard format, but have not sought to establish our thinking on that of the contributors. As such, we must confess that we do not always agree with either some of the methodology employed, or the interpretation of all results. We strongly suspect, that many of the studies could have been done in a superior fashion, but because of either the limitations inherent in any clinical study, or the naivete of the investigator, the methods employed were less than what would otherwise be scientifically acceptable. We therefore exort the reader to examine each series with care, and draw in effect, his own summary table.

If this present volume serves any purpose, it must be two-fold: One, to inform those who heretofore have not been aware of the spinal actions of these opiate compounds and their use as an epidural or intrathecal therapy; and secondly, to alert those who are so knowledgeable to the likely problems which are associated with any new technique. It is perhaps thought that because local anesthetics in the cord are not commonly associated with many supraspinal signs of actions or peripheral side effects that opiates may also be of the same category. The differing physico-chemical characteristics and mode of action, preclude an across the board comparison of these two different pharmacological interventions.

There have been reported in this volume and in the literature, cases of life threatening respiratory depression. It is quite likely that what is reported may be the tip of an ice berg. The use of spinal opiates, while recommended under many conditions, must not be treated lightly. It cannot be assumed the drugs which have the ability to alter spinal function in so profound a fashion can be thought of as trivial. The benefits, however, which accrue from such a powerful addition to the therapeutic regimen, makes it worthwhile to consider this procedure.

In sum, we, the editors, would point out that the use of spinal opiates that has developed so explosively, with what appears to be great promise, is only the beginning of what will likely be a revolution in somatic pain therapy. As indicated above, opiates are not the only system within the spinal cord which modulate sensory transmission. Other systems, no doubt many yet undefined, may offer even more specific pharmacological manipulations. *The rational advances in pain therapy, must be preceded not by random injection of drugs of every sort into the spinal space, but by concerted efforts to understand – at the most basic level – spinal function.* Investigations into the pharmacology and physiology of spinal transmission is an imperative which we must all obey. The advantages and potential advances are without question potentially staggering in their implications for the control of pain.

January 1982

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