A importância do pH intracelular no tratamento do câncer

The relevance of tumour pH to the treatment of malignant disease.


Abstract

The wide range of tumour pH values that have been determined in human tumours is shown in Fig. 4. It can be seen that tumour pH values may be very low, or may fall in the same range as the values found in normal tissues. This means that pH-mediated modification of therapeutic effectiveness will be patient specific, rather than a general phenomenon. That the pH of the cellular environment might influence the effectiveness of various therapeutic agents is not a new idea. The data published in this field to date concerning such effects have been discussed extensively and are summarized in Table IV. Here we can see that low pH leads to decreased cell survival following treatment with hyperthermia, radiotherapy combined with hyperthermia, radiosensitizers and various chemotherapeutic agents. Conversely, low pH affords some protection against radiation and some drugs. Most of these data were, of necessity, derived from in vitro studies. In vivo studies are in most cases not feasible due to the difficulty of isolating the effect of one selected factor. Low tumour pH is, in vivo, generally assumed to be closely interlinked with tissue hypoxia and low blood-flow levels, each of which may individually influence the experimental outcome. Moreover, most of the aforementioned in vitro studies were conducted under well-oxygenated conditions. As previously mentioned, euoxic cells can, under certain conditions, maintain a pH gradient over the cell membrane. This collapses with the onset of hypoxia, leading to intracellular acidification. Low oxygen levels have been shown to be characteristic of many tumours. Within these limitations it is thus evident that tumour pH values could have far-reaching consequences for therapy. If the in vitro findings should prove to be relevant to the clinical situation various applications are possible. Pre-selection of patients less likely to respond to certain (toxic) chemotherapeutic agents, or conversely selection of agents that are more likely to be effective in the pH range of the tumour to be treated are two examples. Alternatively, the exploitation of low tumour pH values is a possibility. Agents that form or release toxic derivatives in areas of low pH, e.g., pH-sensitive liposomes, will work selectively in such areas. Tumour selective therapy may also be possible in patients with higher tumour pH values if the tumour pH can be lowered. This has been
achieved experimentally by the administration of hyperthermia at temperatures above 42 degrees C, or by the administration of glucose. (ABSTRACT TRUNCATED AT 400 WORDS)

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