Effects of anticancer drug docetaxel on the structure and function of the rabbit olfactory mucosa

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Docetaxel (DCT) is an anticancer drug which acts by disrupting microtubule dynamics in the highly mitotic cancer cells. Thus, this drug has a potential to affect function and organization of tissues exhibiting high cellular turnover. We investigated, in the rabbit, the effects of a single human equivalent dose (6.26 mg/kg, i.v.) of DCT on the olfactory mucosa (OM) through light and electron microscopy, immunostaining, TUNEL assay and the buried food test for olfactory sensitivity. On post-exposure days (PED) 5 and 10, there was disarrangement of the normal cell layering in the olfactory epithelium (OE), apoptotic death of cells of the OE, Bowman’s glands and axon bundles, and the presence (including on PED 3) of blood vessels in the bundle cores. A decrease in bundle diameters, olfactory cell densities and cilia numbers, which was most significant on PED 10 (49.3%, 63.4% and 50%, respectively), was also evident. Surprisingly by PED 15, the OM regained normal morphology. Furthermore, olfactory sensitivity decreased progressively until PED 10 when olfaction was markedly impaired, and with recovery from the impairment by PED 15. These observations show that DCT transiently alters the structure and function of the OM suggesting a high regenerative potential for this tissue.

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1. Introduction

The olfactory mucosa (OM) is a chemoreceptor structure located in the nasal cavity, which functions in detecting and discriminating between a myriad of odors (Buck and Axel, 1991; Liberles and Buck, 2006). A detailed morphological description of the OM is available in several of our previous papers (Kavoi et al., 2010, 2012a,b). In brief, the OM comprises an olfactory epithelium (OE) having three principal cell types namely, olfactory receptor neurons, supporting cells and basal cells, and an underlying lamina propria containing bundles of olfactory cell axons, Bowman’s glands and vasculature. In the lamina propria, the axon bundles are surrounded externally by olfactory nerve fibroblasts while their constituent fascicles are encircled by specialized glial cells known as olfactory ensheathing cells (Doucette, 1990; Field et al., 2003; Barnett and Riddell, 2004, Franssen et al., 2007). The bundles project to the olfactory bulb where the fibroblastic envelope and the sheath of olfactory glial cells open out to allow axons from different fascicles to mingle and converge onto mitral and tufted cells (Valverde et al., 1992; Kasowski et al., 1999; Herrera et al., 2005). In histological sections, the OE present three zones named from the apical surface as the free zone, non-nuclear zone and nuclear zone, and with the latter zone being organized into an uppermost layer of elongated nuclei of supporting cells, a middle layer of rounded nuclei of olfactory cells and a lower layer of basal cells nuclei (Burkitt et al., 1993). Replacement of neuronal and non-neuronal cells lost during normal turnover or injury is by rapid division of the OE basal (progenitor) cells, a process that takes place throughout the life of an animal (Calof et al., 1996; Jang et al., 2007; Iwai et al., 2008).

In epithelial tissue, microtubules play a crucial role in the establishment of cell polarity, in controlling differentiative processes and in cell turnover (Yap and Manley, 2001; Janke and Bulinski, 2011). Microtubules serve other functions which include intracellular transport, organelle positioning and change in cell shape (Rodríguez et al., 2003; Tran et al., 2007). In neuronal cells, microtubules are essential for achieving a high degree of morphological

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