Substance P

Substance P (SP) is an undecapeptide (a peptide composed of a chain of 11 amino acid residues) member of the tachykinin neuropeptide family. It is a neuropeptide, acting as a neurotransmitter and as a neuromodulator.

Substance P and its closely related neurokinin A (NKA) are produced from a polyprotein precursor after differential splicing of the preprotachykinin A gene. The deduced amino acid sequence of substance P is as follows:

Arg Pro Lys Pro Gln Gln Phe Phe Gly Leu Met (RPKPQQFFGLM) with an amidation at the C-terminus. Substance P is released from the terminals of specific sensory nerves. It is found in the brain and spinal cord and is associated with inflammatory processes and pain.

A study revealed that the NK-1 receptor is overexpressed in GB, suggesting that substance P (SP) may serve as a ligand. A variety of radioisotopes, beta- (131I, 90Y, or 177 Lu) and alpha emitters (213Bi, 225Ac, or 211At), with different physical properties were tested for treatment. Alpha particles have many advantages over beta radiation such as short range with higher linear energy transfer. According to that characteristic, it is extremely dose delivered to the targeted cells, while reducing harm to nearby healthy tissue. Additionally, the biological effect of alpha radiation is independent of the cell cycle phase, cell oxygenation and O-6-methylguanine-DNA methyltransferase (MGMT) gene promoter methylation status. In this article, we summarize the experience with local treatment of primary and secondary GBs with locally used radioisotopes such as [213Bi]Bi-DOTA-SP or [225Ac]Ac-DOTA-SP [1)].

Previously Lorente et al. from Santa Cruz de Tenerife found higher serum substance P concentrations at day 1 of a malignant middle cerebral artery infarction (MMCAI) in non-surviving than in surviving patients. Thus, the objective of a study was to determine whether serum substance P levels during the first week of MMCAI could predict mortality.

They included patients with MMCAI defined as computed tomography findings of acute infarction in at least of 50% of the territory and Glasgow Coma Scale ≤8. They determined serum concentrations of substance P on days 1, 4 and 8 of MMCAI. Thirty-day mortality was the study end-point.

Serum substance P concentrations at days 1 ($p < .001$), 4 ($p < .001$), and 8 ($p = .001$) of MMCAI in non-surviving ($n = 34$) were higher than in surviving patients ($n = 34$). Receiver operating characteristic analyses showed that serum substance P concentrations at days 1, 4, and 8 of MMCAI had an area under curve (95% confidence intervals) to predict 30-day mortality of 0.77 (0.66-0.87; $p < .001$), 0.82 (0.69-0.91; $p < .001$) and 0.85 (0.72-0.94; $p < .001$) respectively.

The two new findings of the study are that non-surviving MMCAI patients showed higher serum substance P levels at day 1, 4 and 8 than surviving and that those levels could predict 30-day mortality [2)].

1)
Kunikowska J, Morgenstern A, Pełka K, Bruchertseifer F, Królicki L. Targeted alpha therapy for

glioblastoma. Front Med (Lausanne). 2022 Dec 16;9:1085245. doi: 10.3389/fmed.2022.1085245. PMID: 36590948; PMCID: PMC9800503.

2)

Lorente L, Martín MM, Pérez-Cejas A, González-Rivero AF, Argueso M, Ramos L, Solé-Violán J, Cáceres JJ, Jiménez A, García-Marín V. High serum substance P levels and mortality after malignant middle cerebral artery infarction. J Crit Care. 2020 Jan 20;57:1-4. doi: 10.1016/j.jcrc.2020.01.022. [Epub ahead of print] PubMed PMID: 31991332.