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Curcumin for radiation induced enteritis: A review article

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Abstract

Radiation therapy is important treatment modality in various abdominal and pelvic malignancies. Acute and chronic side effects are reported due to radiation therapy. Radiation enteritis is one of them in those patient receiving abdominal and pelvic radiation. It is a complex interplay of various pathophysiological processes ranging from inflammation to free radical damage of lining of the large and small bowel. Patients suffering from acute enteritis may complain of nausea, vomiting, abdominal cramping, tenesmus, and watery diarrhea. Newer form of oral curcumin (Micronized and Nano Curcumin) is an emerging pharmaco-dietary interventions, capable of minimizing the radiation induced damage to the biological system and improve the quality of life of patients.

Keywords: Curcumin, Radiation enteritis, Micronized and Nano-form curcumin, Therapeutic effect

Introduction

Radiation therapy is a very important modality for treatment of most of the cancer patients, either for cure or and for the palliative management of other incurable malignancies. About 60% of patients need Radiotherapy either alone or in combination of chemotherapy and/ or surgery.(1) Sensitive tissues like bone marrow and intestinal mucosa, having rapid cell renewal are prone to the toxicity of ionizing radiation. Radiation enteritis is a complex interplay of various pathophysiological processes ranging from inflammation to epithelial regeneration and free radical damage epithelial cells, like those lining the large and small bowel.(2) Crypt cell wall necrosis can be observed 12 to 24 hours after a daily dose of 1.5 to 3 Gy. Progressive loss of cells, villous atrophy, and cystic crypt dilation occur in the ensuing days and weeks. Patients suffering from acute enteritis may complain of nausea, vomiting, abdominal cramping, tenesmus, and watery diarrhea. With diarrhea, the digestive and absorptive functions of the gastrointestinal (GI) tract are altered or lost, resulting in malabsorption of fat, lactose, bile salts, and vitamin B_{12}. Symptoms of proctitis—including mucoid rectal discharge, rectal pain, and rectal bleeding (if mucosal ulceration is present)—may result from radiation damage to the anus or rectum. Acute enteritis symptoms usually resolve 2 to 3 weeks after the completion of treatment, and the mucosa may appear nearly normal. Only 5% to 15% of the patients who receive abdominal or pelvic irradiation will develop chronic radiation enteritis. The initial signs and symptoms occur 6 to 18 months after radiation therapy. Signs and symptoms include the following: Colicky abdominal pain. Bloody diarrhea. Tenesmus Steatorrhea weight loss. Less common are bowel obstruction, fistulas, bowel perforation, and massive rectal bleeding.(3) Thus it's a challenge to develop pharmaco-dietary interventions, capable of minimizing the radiation induced damage to the biological system.

Modern research has found that effectiveness of turmeric is because of a natural compound it contains: Curcumin. By extracting curcumin from turmeric, we have an even more powerful way to treat disease. Curcumin is a diarylheptanoid. It is the principal curcuminoid of the popular South Asian spice turmeric, which is a member of the ginger family (*Zingiberaceae*). Turmeric's other two curcuminoids are desmethoxycurcumin and bis-desmethoxycurcumin.
The curcuminoids are natural phenols that are responsible for the yellow color of turmeric.(4) Curcumin is a considerably promising compound, its poor water solubility and fast degradation profile make it compromise over its bioavailability way below the threshold level on administration. Over a period of time, a lot of emphasis has been given to improve the bio-distribution of native curcumin, enhancing the absorption of curcumin with micronization and nano-range formulation has significantly improved its therapeutic efficacy. These attempts have given a strong platform to reap all the biological benefits from this phytodrug, which was not significantly plausible earlier.(5)

Because of its anti-inflammatory activity, as well as its ability to kill tumor cells, increase activity of protective antioxidants such as glutathione, and modulate tumor growth cell factors, curcumin is effective against hundreds of diseases.(6) Curcumin is also a potent antioxidant, able to neutralize reactive free radicals. Its ability to neutralize free radicals is extraordinarily strong. Further it reduces inflammatory compounds in the intestines, this review article intends to study the benefits of administration of curcumin to patients suffering from Radiation induced enteritis.

Aim

The aim of this review of literature was to summarize the clinical efficacy and safety of oral curcumin therapy in prevention of radiation induced enteritis.

Methods

A systemic review was done from Medline, Embase and Pubmed and textbooks on herbal medicine.

Review of Literature

Radiation enteritis is a bowel pathology resulting from toxic effects of radiotherapy on the bowel mucosa and vasculature. Approximately 5 - 15% of patients treated with radiotherapy (usually > 4500cGy) develop chronic radiation enteropathy. Curcumin is known to reduce the inflammation related side effects when administered in micronized form.[7]

Laboratory research shows that curcumin is a pleiotropic molecule possibly capable of interacting with molecular targets involved in inflammation.[8] In vitro, curcumin modulates the inflammatory response by down-regulating the activity of cyclooxygenase-2, lipoxygenase, and inducible nitric oxide synthase enzymes and inhibits several other enzymes involved in inflammation mechanisms.[8,9] Curcumin and turmeric are considered safe under conventional daily consumption amounts for most adults.[7] Schiborr C *et al* has shown both, the micronized powder and in particular the liquid micelles formation significantly improves its bioavailability without altering the safety parameters.[10]

Goel *et al* stated that curcumin has also been shown to increase the activity of cancer drugs and to decrease drug resistance in cancer cells.[6] Additionally, it protects normal cells from the toxic effects of chemotherapy drugs and radiation treatments. It has the potential to reduce the inflammation related side effects of Radiation, particularly radiation induced enteritis.

Shehzad *et al* investigated the ways of increased bioavailability, precise molecular targeting in cancer chemoprevention in clinical trials.[11]

Nevertheless, widespread clinical application of this relatively efficacious agent in cancer and other diseases has been limited due to poor aqueous solubility, and consequently, minimal systemic bioavailability. Micronized and Nanoparticle-based drug delivery approaches have the potential for rendering hydrophobic agents like curcumin dispersible in aqueous media, thus circumventing the pitfalls of poor solubility.[12] In the course of the past decade, the field of drug delivery has been revolutionized with the advent of nanotechnology, wherein biocompatible nanoparticles have been developed as inert systemic carriers for therapeutic compounds to target cells and tissues. A recent example of the impact of nanomedicine in drug delivery is underscored by the success of Abraxane™, an albumin nanoparticle conjugate of paclitaxel, and the first FDA-approved anti-cancer agent in this emerging class of drug formulations.

Conclusion

The poor solubility of the curcumin limits its therapeutic efficacy but micronized and nano-curcumin preserves the properties of curcumin and ensures that it reaches the affected tissue to show its therapeutic effect efficiently.

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