Efficacy of Curcumin in the Treatment of Advanced Pancreatic Ductal Adenocarcinoma Compared to Sole Gemcitabine Chemotherapy

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Abstract

Pancreatic ductal adenocarcinoma (PDAC) is a leading cause of cancer death in both men and women. Due to the difficulty of diagnosing this malignancy until it has progressed to an advanced stage, treatment is often difficult, expensive and ineffective. The first line treatment for PDAC is Gemcitabine chemotherapy. However, due to its extensive side effect profile and the early chemo-resistance the PDAC cells develop against Gemcitabine, the need for alternative therapeutic methods to manage treatment is necessary. Therefore, this review analyzes if in individuals with advanced pancreatic ductal adenocarcinoma [P], does the addition of curcumin with the standard Gemcitabine chemotherapy [I] provide reduction in disease progression without causing additional adverse reactions [O] when compared to sole Gemcitabine chemotherapy [C]?

Introduction

Pancreatic Ductal Adenocarcinoma (PDAC)

Overview

- 4th leading cause of cancer related death in the world
- 5-year survival ~8.5%
- In 2018 alone, there was ~55,440 new cases with ~44,330 deaths

Symptoms:

- upper abdominal pain radiating to the back, nausea, vomiting, unintended weight loss, inability to digest fatty foods, or jaundice

Treatment:

- First line treatment is Gemcitabine Chemotherapy
- Surgical resection only if diagnosis at early stage
- even after potentially curative resection, disease relapse occurs in 80% of individuals

Curcumin

- derived from turmeric
- demonstrated to have antioxidant, anti-inflammatory and anticancer properties against various types of cancers.
- minimal toxicity and its safety is FDA approved

Methods

Literature Search Performed in October 2018

- PubMed, Google Scholar, and Cochrane Library
- Search Terms: “pancreatic cancer AND curcumin” or “pancreatic cancer AND curcumin AND Gemcitabine”

Articles where selected based on relevance to the research question, publication date, results, and studies based on human subjects.

Results

There is hopeful evidence that curcumin may be efficacious in disease management in patients with advanced pancreatic adenocarcinoma. All studies demonstrated an **improvement in overall survival time** with curcumin administration when compared to the survival time with sole Gemcitabine chemotherapy. There was **only two studies in which no participant saw a partial or complete tumor response**, however stable disease status was achieved (Kanai et al, 2011 and Kanai et al, 2013).

Bioavailability of curcumin was measured in 3 out of the 5 studies, but **only one study was able to achieve dose dependent levels of curcumin** (Kanai et al, 2013). This study used curcumin in a more bioavailable formulation compared to other studies.

Of the 2 studies that evaluated quality of life, **only one saw statistically significant improvement in fatigue and functioning-associated quality of life scores** (Kanai et al, 2013). Other studies did show reduced side effects with curcumin use when compared to sole Gemcitabine therapy. However, 3 studies had at least 1 participant **drop out due to curcumin related toxicity**.

Overall, tumor marker levels or serum proinflammatory cytokine levels had no correlation to tumor response.

Table 1. Comparison Table

Study	Disease State at Baseline	Overall Survival Time	Tumor Response	Systemic Curcumin amounts (Bioavailability)	Toxicity due to Curcumin Administration
Dhillon et al (2008)	Varied	S	S	NS	NS
Epellbaum et al (2010)	Previously untreated advanced or metastatic disease	S	S	n/a	S
Kanai et al (2011)	Resistant	S	NS	NS	NS
Kanai et al (2013)	Resistant	S	NS	S	S
Pastorelli et al (2018)	Varied	S	S	n/a	S

Key: S= significant. NS= not significant n/a= not applicable

Discussion

Studies found some degree of efficacy in the use of curcumin in the treatment of PDAC compared to sole Gemcitabine chemotherapy.

Strengths:

- similar inclusion criteria
- consistent data analysis
- similar length of data collection
- 5/6 studies evaluated the addition of curcumin to Gemcitabine during the study period

Limitations:

- small sample sizes
- lack of double-blind studies
- Varied study designs
- different formulations of curcumin utilized

Conclusion

The study results are **positive**, however, **more research is needed** in order to make a definitive conclusion. For patients suffering from advanced pancreatic ductal adenocarcinoma, curcumin appears to be a **reasonable and potentially efficacious addition** to the standard first-line chemotherapy, Gemcitabine, regardless of disease state. Curcumin has shown to provide disease stabilization. Some major drawbacks to this therapy is it’s lack bioavailability and the curcumin related toxicity experienced by participants.

Evidence is **insufficient to change current practice**, but there is enough positive results to **support and encourage future research**. Further studies with a more bioavailable curcumin formula that increases serum curcumin levels in a dose depended way should be investigated and performed. This could potentially provide better tumor response and quality of life, and improved overall survival rate.