International Research Journal of Pharmacy and Medical Sciences
ISSN (Online): 2581-3277

Unveiling the Significance of Stem Cell Therapy for Gastric and Peptic Ulcer Patients

G. Kinnera Ratna Sri[1], M. Ganga Raju[2], N V L Suvarchala Reddy V[3], K. Lakshmi Sravani[4]
D. Gowthami[5], P. Prasoona[6], Y Ch Hashan reddy[7]
[1,2,3]Department of Pharmacology, Gokaraju Rangaraju College of Pharmacy, Hyderabad, Telangana, India, 500090
[4,5,6,7]Gokaraju Rangaraju College of Pharmacy, Hyderabad, Telangana, India, 500090
E mail: [1]kinneraratnasri@gmail.com

Abstract*—Globally, ulcers are identified as a substantial healthcare burden that requires comprehensive management solutions in order to maximize patient outcomes. Well established treatments, such as antibiotic therapy for the eradication of Helicobacter pylori, mucosal protective medicines, histamine-2 receptor antagonists (H_2RAs), and proton pump inhibitors (PPIs) may provide long term side effects as they were used as a long term therapy. In order to minimize the side effects of long term use, complementary methods such as non-pharmacological therapies like lifestyle changes, endoscopic procedures, and surgical options were currently gaining the most prominent attention. In addition, recently stem cell therapy is gaining more attention from the researchers as it has a more significant quality of regeneration. Stem cell therapy is commonly used to repair or replace damaged cells or tissues, but it can also be utilized to prevent damage. Stem cell therapy involves the use of mesenchymal stromal stem cells (BSC) derived from bone marrow and adipose tissue-derived mesenchymal stromal cells (ASC). However, adipose-derived mesenchymal stem cells are easily accessible in large quantities with little invasive intervention. These cells are very flexible and can develop in vitro into a variety of cell types. This review offers a summary of the significance of stem cell therapy in treating gastric ulcer and provides insights in to pros and cons of stem cell therapy in gastric ulcer healing*.

Keywords— *Adipose derived mesenchymal stromal stem cells; bone marrow derived mesenchymal stromal stem celsl; gastric ulcer; peptic ulcer*.

I. INTRODUCTION

Peptic ulcers are basically gastrointestinal ulcers caused by a tear in the lining of the stomach or the upper part of the intestine. At its worst, this illness has the potential to produce severe pain or discomfort. When it grows worse, there's also the risk of perforation. Peptic ulcer illness can be treated with a variety of drugs, although some individuals may not respond to them at all. Surgery may be a possibility in more serious cases. Pre-clinical research on animals has demonstrated that using stomach stem cells can quicken the healing process for peptic ulcers. Additionally, it will go over the standard care treatment. Patients experiencing excruciating stomach ulcers benefit from stem cell therapy. According to some study, age is a major risk factor for stomach ulcers, but other factors like diminished body's capacity to repair wounds also seem to be significant. Stomach stem cells are the cells that are mending the lining. Peptic ulcer disease is a frequent condition with a lifetime frequency of 5–10% and an annual incidence of 0.1–0.3% in the general population [1].

Gastric acid damages gastro-duodenal mucosa and cause mucosal erosion, which leaves the underlying tissues vulnerable to the digesting action of gastro-duodenal secretions, leading to peptic ulceration. Traditionally, a hypersecretory acid environment, certain dietary variables, and stress were associated with this illness. Bleeding and perforation are among the complications of peptic ulcer disease, and blockage from chronic fibrotic illness is becoming less common due to advancements in medical care. Hemorrhage is by far the most common complication of peptic disease, according to a recent review on the epidemiology of complicated peptic ulcer disease[2]. The annual incidence of hemorrhage in the general population is reported to range from 0.02 to 0.06%, with an average 30-day mortality weighed by sample size of 8.6%. Perforation incidence is reported to range from 0.004 to 0.014% annually, with an average 30-day mortality weighed by sample size of 23.5%. Perforation is the most common indication for emergency surgery and accounts for around 40% of ulcer-related mortality, despite being less common (perforation: bleeding ratio: approximately 1:6) [3]. Current therapy includes antacids, histamine (H_2) blockers, proton pump inhibitors (PPIs), medications to protect and strengthen the mucous lining of the stomach and antibiotics to treat *H. pylori* if identified. Recently, there is new focus on stem cells therapy to treat peptic ulcers. However, current review mainly focussed on treatment of peptic ulcer with the help of stem cell therapy.

II. EPIDEMIOLOGY OF PEPTIC ULCER

Before 19th century, stomach ulcers were an uncommon condition. The incidence of acute perforations of stomach ulcers in young girls was first identified back in early 1800s. Peptic ulcer illness frequency was increased in both men and women during 19th century [4]. The disease affects men and women equally in west; however, it affects men 18 times more frequently than women in India. It is hard to get precise data on disease incidence in a large growing nation like India, and regional variations are inevitable. Peptic ulcers are more common in Jammu and Kashmir and in Southern India followed by north India, with relatively lesser frequency in the East and North East [5]. Due to the high consumption of rice as a

G. Kinnera Ratna Sri, M. Ganga Raju, N V L Suvarchala Reddy V, D. Gowthami, Y Ch Hashan reddy, K. Lakshmi sravani, and P. Prasoona, "Unveiling the Significance of Stem Cell Therapy for Gastric and Peptic Ulcer Patients," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 7, Issue 4, pp. 85-91, 2024.

staple food in South India, the incidence of stomach ulcers may be higher in South India than in North India [6, 7]. For men and women alike, the lifetime risk of getting a peptic ulcer is approximately 10% and 4%, respectively. A prevalence of 2 to 6% for women and 6 to 14% for men was discovered by autopsy research and biopsy. For gastric ulcers, the male to female ratio is 2:1 and for duodenal ulcers, it is 3:1[8].

Due to its increased frequency in elderly patients, gastric ulcers have a higher death rate than duodenal ulcers[9, 10, 11]. The incidence of duodenal ulcers was roughly 2 in 1000 men and 0.9 in 1000 women in young Norwegians. Whereas, the incidence of gastric ulcers was roughly 1.5 in 1000 men and 0.9 in 1000 women [12]. The incidence of gastric ulcers was approximately 1.5 times higher than that of duodenal ulcers in Japan, but the male to female ratio for peptic ulcers was 2:1 [13]. The ratio is five times higher; in certain regions of India, it is as high as 32:1 [14].

One of the main causative factors of peptic ulcers is H. pylori infection. H. pylori infection is the cause of almost 90% of duodenal ulcers and 70% of stomach ulcers [15, 16]. The frequency of infection varies greatly throughout ethnic groups in various societies. Australians of southern European descent have greater infection rates than Australians of Anglo-Celtic ancestry, whereas white Americans have lower infection rates than black Americans[17]. According to a study by Drumm and colleagues, the specific antibody was found in 74 percent of parents and 82 percent of siblings of children infected with H. pylori. These findings indicated a high degree of oral or fecal oral transmission of this infectious organism from person to person[18, 19]. Research from India indicates that between 75% and 90% of ulcers resolve with antibiotic treatment which eradicate the H. pylori bacteria[20]. Peptic ulcers disease (PUD), which includes duodenal and stomach ulcers, is currently the most common gastrointestinal illness. An estimated 15,000 people die from PUD-related causes each year, and three out of every 1000 people suffer from peptic ulcer disease. Bleeding is linked to 20% of ulcer episodes [21, 22].

III. Risk Factors

Gastric ulcers are primarily caused by Helicobacter pylori infection and the use of nonsteroidal anti-inflammatory drugs (NSAIDs). H. pylori, a bacterium that colonizes the stomach lining, leads to chronic inflammation and ulcer formation, and is found in 60-80% of patients with gastric ulcers globally. NSAIDs, including aspirin and ibuprofen, inhibit the production of prostaglandins, which protect the stomach lining, thereby increasing the risk of ulcers. Other significant risk factors include smoking and alcohol consumption, which can exacerbate mucosal damage and delay healing. Additionally, stress and a diet high in spicy and acidic foods can contribute to the development of gastric ulcers, although these factors are less significant compared to H. pylori infection and NSAID use. Genetic predisposition also plays a role, with some individuals being more susceptible to ulcer formation. Socio-economic factors, such as poor living conditions and limited access to healthcare, further increase the risk, especially in developing countries where H. pylori prevalence is high [23].

IV. Pathophysiology

Gastric ulcers develop through a sequence of events triggered by certain risk factors such as the use of nonsteroidal anti-inflammatory drugs (NSAIDs), alcohol, and coffee or tea as mentioned in fig. 1. NSAIDs inhibit the production of prostaglandins, which help maintain the protective mucus lining of the stomach, while alcohol increases stomach acid production and directly irritates the stomach lining. Both caffeinated and decaffeinated coffee can stimulate acid production, contributing to mucosal damage. This leads to an excessive secretion of hydrochloric acid (HCl) and a decrease in mucus secretion, disrupting the balance between aggressive and protective factors in the stomach. As the mucus membrane breaks down, the underlying tissue is exposed to stomach acids and digestive enzymes, causing inflammation and damage to the gastric mucosa. Continuous exposure results in the formation of gastric ulcers, which are open sores that can cause pain and may lead to complications such as bleeding, perforation, and obstruction.

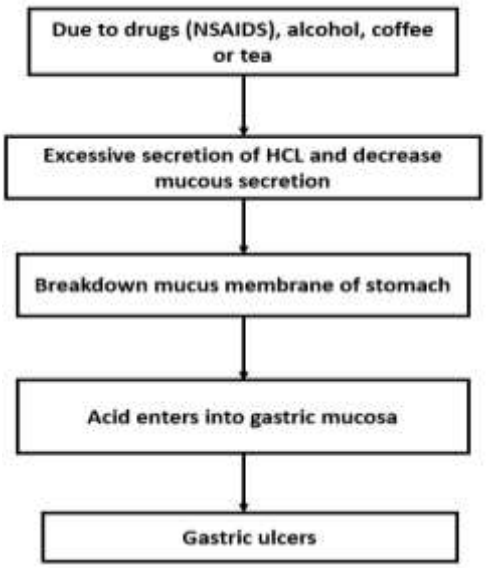

Fig. 1. Pathophysiology of gastric ulcers

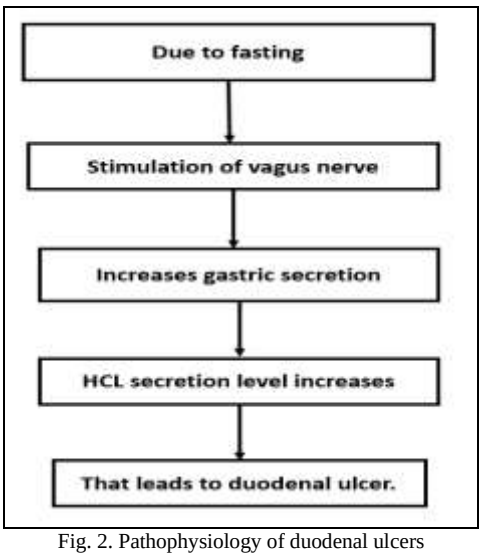

Fig. 2. Pathophysiology of duodenal ulcers

G. Kinnera Ratna Sri, M. Ganga Raju, N V L Suvarchala Reddy V, D. Gowthami, Y Ch Hashan reddy, K. Lakshmi sravani, and P. Prasoona, "Unveiling the Significance of Stem Cell Therapy for Gastric and Peptic Ulcer Patients," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 7, Issue 4, pp. 85-91, 2024.

Duodenal ulcers develop through a series of physiological responses that begin with fasting. When fasting occurs, the vagus nerve is stimulated, which increases gastric secretion. This heightened gastric activity leads to a significant increase in the secretion of hydrochloric acid (HCl). The elevated levels of HCl then contribute to the development of duodenal ulcers by damaging the lining of the duodenum, the first part of the small intestine as mentioned in fig 2 [24, 25].

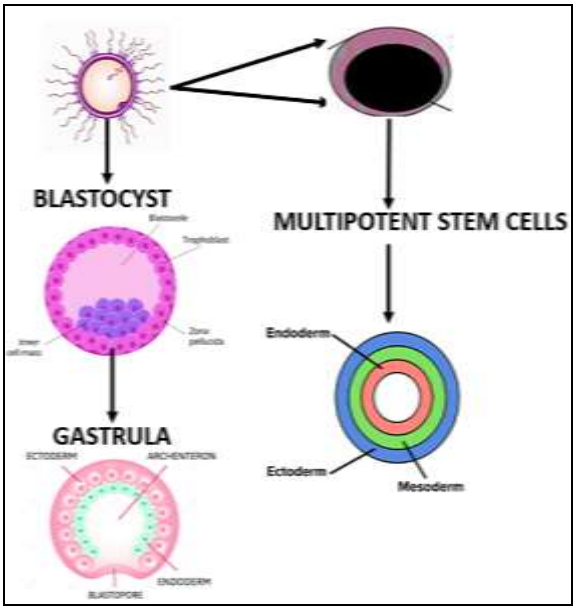

Fig. 3. Derivate of Stem Cells Natural embryo development

V. Stem Cells

Numerous stem cells are produced in the mortal body; they hold great pledge for remedial operations in the future, including rejuvenescence. Two prerequisite features must be present in a cell for it to be classified as a "stem cell". In order to produce seed that are identical to their parent cell, stem cells must first retain the capacity for tone- renewal. This specific also applies to cancer cells, which divide aimlessly while stem cell division is well controlled. It's pivotal that stem cells need to have the capacity to separate into a specific cell type that ultimately becomes an element of a healthy person[26]. There are multitudinous cell types that fall under the general term "stem cell". Traditionally, stem cells are classified as either "embryonic" or "adult" grounded on the experimental stage of a healthy person from which they appear. On the other hand, adult stem cells are most commonly known as physical “stem cells”, which means “from the body” [27] and they can separate into any form of cell in the body. Pluripotent stem cells are only set up in embryos for a fairly brief time during normal development before transubstantiating into multipotent stem cells, which are more technical stem cells that ultimately give rise to the body's technical apkins as mentioned in fig 3. These more defined multipotent stem cells are available in multiple subtypes; some can separate into only endoderm, mesoderm, or ectoderm cells, while others can separate into only cells of a specific tissue. In another way, pluripotent cells have the capability to separate into multipotent stem cells, which in turn suffer numerous divisions to come indeed more technical cells, eventually enabling them to come any type of cell in the body.

VI. Stem Cell Therapy

Due to unfavorable development of strange solid tumors known as teratomas in numerous early animal trials, pluripotent stem cells have not yet been employed therapeutically in humans. Mixture of cell types from all early germ layers makes up teratomas. This proliferation capacity is limited by the use of pluripotent cells transformed to a more mature phenotype in later successful animal research. Animals have been successfully treated using cells that are derived from pluripotent cells.

For example, insulin-producing cells that are sensitive to glucose levels have been created and used to treat animals with diabetes. Additionally, the development of new myelinated neurons or retinal epithelial cells has been used to cure animals suffering from acute spinal cord injuries or visual impairment, respectively. The FDA and commercial companies are presently negotiating the prospect of moving forward with human studies. Additional research on animals has been done to cure a variety of illnesses, including heart failure, muscular dystrophy, and Parkinson's disease[28,29,30].

Incorporation of freshly created beating cardiac myocytes into the myocardium to provide higher force, scientists expect that stem cell therapy can improve heart function. After being transplanted into animals, patches of cardiac myocytes made from human embryonic stem cells can develop into viable human myocardia, with some even exhibiting electrical integration[31, 32, 33]. Insulation of damaged mouse hearts with human embryonic stem cell-derived cardiac myocytes resulted in a small improvement in ventricular function. Although the exact mechanisms underlying the increase in function are unknown, direct integration of newly beating heart cells may only be one factor. More likely, it is because paracrine effects help other heart cells already in existence.

VII. Multipotent Stem Cells

Since 1960s, leukemia, myeloma, and lymphoma have been treated with multipotent stem cells taken from bone marrow. The significance of these cells in the treatment of blood malignancies is readily apparent because the cells there give rise to lymphocytes, megakaryocytes, and erythrocytes. There have been some recent reports of advances in the treatment of other diseases with bone marrow-derived cells. For example, mesenchymal stem cells, which give rise to bone and cartilage, have been used to construct whole joints in mice models[34]. Multipotent stem cells have the potential to treat numerous other illnesses and medical issues in the near future. Clinical trials are being conducted using bone marrow-derived stem cells to treat heart conditions.

VIII. Pluripotent Vs. Multipotent

Both multipotent and pluripotent stem cells offer benefits and drawbacks. One clear therapeutic advantage of pluripotent cells over their multipotent counterparts is their ability to differentiate into any type of cell. In theory, they might be

G. Kinnera Ratna Sri, M. Ganga Raju, N V L Suvarchala Reddy V, D. Gowthami, Y Ch Hashan reddy, K. Lakshmi sravani, and P. Prasoona, “Unveiling the Significance of Stem Cell Therapy for Gastric and Peptic Ulcer Patients,” *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 7, Issue 4, pp. 85-91, 2024.

utilized to treat aging or sick tissues where multipotent stem cells are insufficient. Furthermore, because pluripotent stem cells divide more quickly, they can produce more functional cells overall.

On the other hand, using autologous multipotent stem cells (stem cells taken from oneself) would not require immune suppressive medications for the course of the graft, in contrast to using donor pluripotent stem cells[35]. One of the main advantages of pluripotent stem cells is their ability to use their own cells. Certain surface proteins on cells or objects are recognized by the immune system as indicators of the host cell's identity and health.

Because autologous, multipotent stem cells bear the patient's unique surface proteins, the host immune system can accept them and prevent an immunological response. Conversely, because pluripotent stem cells are not derived from the host, they do not have the necessary signals to withstand immune system rejection. One potential benefit of iPS cells is the current research efforts to reduce the immunological response triggered by pluripotent cells.

IX. Significance Of Mesenchymal Stem Cells (MSC) In Treating Ulcer

MSCs have been shown to improve the healing of experimentally produced stomach ulcers, autoimmune non-healing gastric ulcers, and radiation gastric ulcers. Bone marrow derived cells (BMDCs) are stem cells that can recruit to sites of tissue injury and inflammation, potentially repairing damaged tissues. However, their surprising adaptability may provide a risk for cancer. BMDCs can help in healing stomach ulcers by developing into vascular endothelial cells, epithelium, and interstitial cells. Although, MSCs are highly proliferative and differentiative in gastric tissue, with promise therapeutic effects, their use in practical therapeutics requires a better understanding of their activity in pathological situations. Study by Yujiro Hayashi and colleagues revealed the activation of angiogenesis in the gastric mucosa by the release of VEGF may have contributed to the rapid healing of gastric ulcers following MSCs transplantation. The potential of MSCs to produce angiogenic factors may also play a role in mediating their advantageous effects, in addition to their differentiation into stomach interstitial cells[36]. In addition, a study by Laila Rashed and Salwa Fayez reported that the process of gastric ulcer healing by administration of MSCs is enhanced due to increased expression of epidermal growth factor (EGF) and Vascular endothelial growth factor (VEGF) by decrease in serum IL1β and TNF-α level[37]. In conclusion, MSCs have the capacity to proliferate into gastric stroma epithelial cells and move to injured mucosal surfaces. Additionally, they have the ability to secrete cytokines and matrix proteins that encourage angiogenesis and cell growth during the repair of gastrointestinal ulcers[38].

X. Adipose-Derivedmesenchymal Stem Cells (AD-MSC)

Compared to Bone marrow-MSCs (BM-MSCs), the isolation of ADMSCs is less invasive and more accessible. It is achieved through liposuction, washing, and enzymatic digestion by collagenase, and centrifugation of adipose tissue. Adipose-derived mesenchymal stem cells (ADMSCs) comprise stem cells capable of differentiating into osteogenic, chondrogenic, and adipogenic lineages. Numerous studies have examined their involvement in differentiating into myocytes, hepatocytes, neural cells, and epithelial cells of the lung, kidney, and skin. Adipose tissue-derived cells have potential for regenerative therapy and are a promising stem cell source for clinical applications. ADMSCs activate regulatory T-cells (Tregs) and suppress Th1, Th2, and Th17 cells via boosting immune-modulatory substances[39].

XI. Healing Effect of Adipose-Derived Mesenchymal Stem Cells On Ulcer

Adipose-derived MSCs show great promise as a therapy for a variety of illnesses. MSCs are used because of their ability to heal damaged tissues while also inhibiting inflammation and fibrosis. In a study by Safaa A. Hassan and colleagues reported that adipose-derived MSCs speed up the healing of gastric ulcers in mice by stimulating cell proliferation to repair ulcer damage and increase angiogenesis, keeping the ulcer site adequately oxygenated[40]. Whereas, a study by Sayed A H and colleagues revealed that combined treatment of ADSCs and pantaprazole can significantly protect against gastric ulcers by balancing oxidants and antioxidants, improving vascularization of gastric tissue through overexpression of the gastric VEGF gene, and reducing inflammation through down-expression of gastric tissue NF-κB, TNF-α and COX-2 genes[41]. In addition, Xia X and colleagues reported that endoscopic submucosal injection of ADMSCs aided in the repair of NSAID-related stomach ulcers by inhibiting inflammatory infiltration and increasing cellular proliferation and angiogenesis. This effect might be a used as a promising alternative for patients with NSAID-related GI ulcers, especially those who suffer the negative effects of long-term use of proton pump inhibitors[42]. Additionally, study conducted by Liu and colleagues suggested that MSCs were administered locally into a mouse model that had a stomach hole. According to this study, MSCs help heal gastrointestinal perforation by granulation tissue regeneration, TGF-β1 production, re-epithelialization, and inflammation inhibition[43]. A different study demonstrated that ADMSCs enhanced the histology of gastric tissue in a model of gastric ulcer brought on by indomethacin and it was demonstrated that the stem cell injection decreased pathological alterations in the morphology of gastric ulcers and returned stomach prostaglandin E2 levels to normal. Additionally, mesenchymal stem cells raise VEGF levels above normal, which speeds up the healing process[44]. In a study where, ADMSCs were applied to aspirin-induced stomach ulcers revealed that gastric fundus glands were fully repaired and the infiltration of inflammatory cells had significantly decreased 72 hours after the AD-MSC transplantation. According to this study, AD-MSCs may be readily extracted from adipose tissue and quickly proliferate in culture media, where they may aid in the repair of stomach ulcers[45].

G. Kinnera Ratna Sri, M. Ganga Raju, N V L Suvarchala Reddy V, D. Gowthami, Y Ch Hashan reddy, K. Lakshmi sravani, and P. Prasoona, "Unveiling the Significance of Stem Cell Therapy for Gastric and Peptic Ulcer Patients," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 7, Issue 4, pp. 85-91, 2024.

XII. Advantages Of Stem Cell Therapy In Treatment Of Ulcers

The special properties of stem cells promote tissue regeneration and healing. Hence, stem cell therapy has a number of potential benefits for the treatment of peptic ulcers which includes[46]

Tissue Regeneration

Stem cells can develop into a variety of cell types, including the lining of the stomach. Stem cells may be able to develop into healthy epithelial cells at the ulcer site, aiding in the repair of damaged tissue.

Lessened Scarring

Stem cell therapy may result in less fibrosis and scarring at the ulcer site as compared to conventional ulcer therapies like drugs or surgery. This is so that tissues can recover and function better because stem cells have the ability to encourage tissue repair without producing an excessive amount of scarring.

Anti-inflammatory Effects

Because stem cells have anti-inflammatory qualities, they may be able to lessen ulcer site inflammation. Stem cells may help resolve the inflammation linked to peptic ulcers by regulating the immune system, which would aid in healing and lessen symptoms.

Enhanced Healing

By encouraging the migration and proliferation of healthy cells to the site of injury, stem cell therapy can hasten the healing of peptic ulcers. This may result in better patient outcomes and a quicker cure of ulcer symptoms.

Minimally Invasive

Stem cell therapy for peptic ulcers may be less invasive than extensive surgical procedures, depending on the mode of administration. By comparison with conventional surgical treatments, this could lead to reduced risk of complications and quicker recovery times.

Personalized Care

Depending on the severity of the ulcer, the patient's medical background, and any underlying problems, stem cell therapy can be customized for each patient. Patient satisfaction can be raised and treatment outcomes can be optimized with this customized strategy.

Potential Long-Term advantages

Stem cell therapy may provide long-term advantages for individuals with peptic ulcers by stimulating tissue regeneration and repair. This may lower the risk of ulcer recurrence and complications related to chronic ulceration, such as bleeding or perforation.

Alternative to traditional Treatments

Stem cell therapy may provide a different therapeutic option with possibly less side effects for patients who do not react to traditional treatments or who significantly experience negative effects from drugs.

Promising Research

Although there is still much to learn about stem cell therapy for peptic ulcers, initial investigations and clinical trials have shown encouraging findings that point to the treatment's possible efficacy in accelerating ulcer healing and reducing associated symptoms. All things considered, stem cell therapy is a promising new approach to treating peptic ulcers, with a number of potential benefits over conventional treatments. To comprehend its effectiveness, safety, and long-term results in clinical settings, more study is necessary.

XIII. Disadvantages of Stem Cells Therapy on Ulcers

Peptic ulcers are among the medical disorders for which stem cell therapy has shown promise; nevertheless, like with any medical intervention, there are drawbacks. The following are some possible disadvantages unique to peptic ulcer stem cell therapy[47].

Limited Research

Although research on stem cell therapy for the treatment of peptic ulcers is still in its early phases, it shows promise. Concerns exist about both its long-term safety and efficacy.

Risk of Tumor Formation

The possibility of unchecked development or tumor formation is one issue with stem cell therapy. Uncontrolled proliferation of stem cells can occasionally result in the development of tumors, including malignant ones.

Immunological Rejection

There's a chance that the transplanted stem cells will be attacked by the immune system, which will perceive them as alien substances. This may result in the transplanted cells being rejected, which would lessen their efficacy.

Ethical Concerns

For certain people or societies, using particular types of stem cells—like embryonic stem cells—raises ethical questions. This may restrict the acceptability and accessibility of specific stem cell treatments.

Cost

If numerous treatments are needed, stem cell therapy may be costly. This therapy option may not be accessible to all patients due to its expense.

Regulatory Obstacles

The approval procedures for stem cell therapies by the authorities can be convoluted and drawn out. Patients who would benefit from treatment may experience delays or limitations as a result of this.

Unknown Long-Term Effects

Because stem cell therapy is still in its infancy, it is unknown what the treatment's long-term effects will be. This

G. Kinnera Ratna Sri, M. Ganga Raju, N V L Suvarchala Reddy V, D. Gowthami, Y Ch Hashan reddy, K. Lakshmi sravani, and P. Prasoona, "Unveiling the Significance of Stem Cell Therapy for Gastric and Peptic Ulcer Patients," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 7, Issue 4, pp. 85-91, 2024.

covers any possible issues or side effects that could appear years after the first round of treatment.

Lack of Understanding

Even with the progress made in the field of stem cell research, there might be unanswered questions about how stem cells function in the body and whether or not they can be successfully employed to cure peptic ulcers. This ignorance could restrict the efficacy of the treatment or result in unanticipated consequences.

To determine whether stem cell therapy is appropriate for treating peptic ulcers, it is critical to assess the potential drawbacks against the benefits and speak with medical experts.

XIV. Conclusion

Numerous treatments are available to patients with stomach and peptic ulcers, but it's critical to diagnose and treat the illness methodically. Risks related to long-term usage of proton pump inhibitors and other medications have lately come under examination. It is unclear whether surgical or pharmaceutical treatment is better for patients with chronic or recurrent stomach ulcers. As such, stem cell therapy might be advantageous for these patients. One new method for treating duodenal and stomach ulcers that are resistant to treatment is MSC transplantation. In addition, mesenchymal stem cell therapy could be a helpful intervention against radiation enteropathy. Further studies have to be done to identify the safety profile and detail mechanisms of stem cell therapy for ulcers.

Acknowledgement

I sincerely thank my head of the department, principal and management of Gokaraju Rangaraju College of Pharmacy for intense support for this review.

References

[1] Lanas A, Chan FK. “Peptic ulcer disease,” *The Lancet*, vol. 390, issue 10094, pp. 613-24, 2017.

[2] Lau JY, Sung J, Hill C, Henderson C, Howden CW, Metz DC. “Systematic review of the epidemiology of complicated peptic ulcer disease: incidence, recurrence, risk factors and mortality,” *Digestion*, vol. 84, issue 2, pp. 102-13, 2011.

[3] Søreide K, Thorsen K, Harrison EM, Bingener J, Møller MH, Ohene-Yeboah M, Søreide JA. “Perforated peptic ulcer,” *The Lancet*, vol. 386, issue 10000, pp. 1288-98, 2015.

[4] Sonnenberg A. “Geographic and temporal variations in the occurrence of peptic ulcer disease,” *Scandinavian Journal of Gastroenterology*, vol. 20, issue (sup110), pp. 11-24, 1985.

[5] Das S, Deka S, Gohain K. “A preclinical study on gastric ulcer protective activity of world’s hottest chilli Capsicum frutenscenes,” *J Clin Diag Res*, vol. 2, pp. 1024-27, 2008.

[6] Das D, Dash D, Mandal T, Kishore A, Bairy KL. “Protective effects of Moringa oleifera on experimentally induced gastric ulcers in rats,” *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, vol. 2, issue 2, pp. 50-5, 2011.

[7] Tovey FI. “Peptic ulcer in India and Bangladesh,” *Gut*, vol. 20, issue 4, pp. 329, 1979.

[8] Sandler RS, Everhart JE, Donowitz M, Adams E, Cronin K, Goodman C, Gemmen E, Shah S, Avdic A, Rubin R. “The burden of selected digestive diseases in the United States,” *Gastroenterology*, vol. 122, issue 5, pp. 1500-11, 2002.

[9] Langman MJ. “Trends in ulcer frequency,” *Postgraduate Medical Journal*, vol. 64, pp. 37-9, 1988.

[10] Til Vis RS, Vuoristo M, Varis K. “Changed profile of peptic ulcer disease in hospital patients during 1969–1984 in Finland,” *Scandinavian journal of gastroenterology*, vol. 22, issue 10, pp. 1238-44, 1987.

[11] Sonnenberg A, Fritsch A. “Changing mortality of peptic ulcer disease in Germany,” *Gastroenterology*, vol. 84, issue 6, pp. 1553-7, 1983.

[12] Johnsen R, Straume B, Førde OH, Burhol PG. “Changing incidence of peptic ulcer-facts or artefacts? A cohort study from Tromsø,” *Journal of Epidemiology & Community Health*, vol. 46, issue 4, pp. 433-6, 1992.

[13] Watanabe Y, Kurata JH, Kawamoto K, Kawai K, Zeman RK. “Epidemiological study of peptic ulcer disease among Japanese and Koreans in Japan,” *Journal of clinical* gastroenterology, vol. 15, issue 1, pp. 68-74, 1992.

[14] Hooi JK, Lai WY, Ng WK, Suen MM, Underwood FE, Tanyingoh D, Malfertheiner P, Graham DY, Wong VW, Wu JC, Chan FK. “Global prevalence of Helicobacter pylori infection: systematic review and meta-analysis,” Gastroenterology, vol. 153, issue 2, pp. 420-9, 2017.

[15] Stenström B, Mendis A, Marshall B. “Helicobacter pylori: The latest in diagnosis and treatment,” *Australian Journal of General Practice*, vol. 37, issue 8, pp. 608, 2008.

[16] Lai LH, Sung JJ. “Helicobacter pylori and benign upper digestive disease,” *Best practice & research Clinical gastroenterology*, vol. 21, issue 2, pp. 261-79, 2007.

[17] Lee A. “The microbiology and epidemiology of Helicobacter pylori infection,” *Scandinavian Journal of Gastroenterology*, vol. 29, issue (sup201), pp. 2-6, 1994.

[18] Drumm B, Sherman P, Cutz E, Karmali M. “Association of Campylobacter pylori on the gastric mucosa with antral gastritis in children,” *New England Journal of Medicine*, vol. 316, issue 25, pp. 1557-61, 1987.

[19] Thomas JE, Gibson GR, Darboe MK, Weaver LT, Dale A. “Isolation of Helicobacter pylori from human faeces,” *The Lancet*, vol. 340, issue 8829, pp. 1194-5, 1992.

[20] Dharmani P, Palit G. “Exploring Indian medicinal plants for antiulcer activity,” *Indian journal of pharmacology*, vol. 38, issue 2, pp. 95-9, 2006.

[21] Lindell G, Celebioglu F, Von Holstein CS, Graffner H. “On the natural history of peptic ulcer,” *Scandinavian journal of gastroenterology*, vol. 29, issue 11, pp. 979-82, 1994.

[22] Del Valle J. “Peptic ulcer disease and related disorders,” *Harrisons principles of internal medicine*, vol. 16, issue 2, pp. 1746, 2005.

[23] Graham DY, Khalaf N. “Peptic ulcer disease,” *Geriatric Gastroenterology*, pp. 1-31, 2020.

[24] Shell EJ. “Pathophysiology of peptic ulcer disease,” *Physician Assistant Clinics*, vol. 6, issue 4, pp. 603-11, 2021.

[25] Bereda G. “Peptic Ulcer disease: definition, pathophysiology, and treatment,” *Journal of Biomedical and Biological Sciences*, vol. 1, issue 2, pp. 1-0, 2022.

[26] Hao T, Chen J, Zhi S, Zhang Q, Chen G, Yu F. “Comparison of bone marrow-versus adipose tissue-derived mesenchymal stem cells for attenuating liver fibrosis,” *Exp Therap Med*, vol. 14, issue 6, pp. 5956–64, 2017.

[27] Gnecchi M, Zhang Z, Ni A, Dzau VJ. “Paracrine mechanisms in adult stem cell signaling and therapy,” *Circ Res*, vol. 103, issue 11, pp. 1204–19, 2008.

[28] Kuptsova N, Chang-Claude J, Kropp S, Helmbold I, Schmezer P, von Fournier D. “Genetic predictors of long-term toxicities after radiation therapy for breast cancer”. *Int J Cancer*, vol. 122, issue 6, pp. 1333–9, 2008.

[29] Dar A, Goichberg P, Shinder V, Kalinkovich A, Kollet O, Netzer N, Margalit R, Zsak M, Nagler A, Hardan I, Resnick I. “Chemokine receptor CXCR4–dependent internalization and resecretion of functional chemokine SDF-1 by bone marrow endothelial and stromal cells,” *Nature immunology*, vol. 6, issue 10, pp. 1038-46, 2005.

[30] Zhao Y, Zhang H. “Update on the mechanisms of homing of adipose tissue-derived stem cells,” Cytotherapy, vol. 18, issue 7, pp. 816–27, 2016.

[31] Baek SJ, Kang SK, Ra JC. “In vitro migration capacity of human adipose tissue-derived mesenchymal stem cells reflects their expression

of receptors for chemokines and growth factors," *Exp Mol Med*, vol. 43, issue 10, pp. 596–603, 2011.
[32] De Ugarte DA, Morizono K, Elbarbary A, Alfonso Z, Zuk PA, Zhu M, Dragoo JL, Ashjian P, Thomas B, Benhaim P, Chen I. "Comparison of multi-lineage cells from human adipose tissue and bone marrow". *Cells tissues organs*, vol. 174, issue 3, pp. 101-9, 2003.
[33] Schäffler A, Büchler C. "Concise review: adipose tissue-derived stromal cells—basic and clinical implications for novel cell-based therapies," *Stem Cells*, vol. 25, issue 4, pp. 818–27, 2007.
[34] Atalay S, Coruh A, Deniz K. "Stromal vascular fraction improves deep partial thickness burn wound healing," *Burns*, vol. 40, issue 7, pp. 1375–83, 2014.
[35] Rehman J, Traktuev D, Li J, Merfeld-Clauss S, Temm-Grove CJ, Bovenkerk JE, Pell CL, Johnstone BH, Considine RV, March KL. "Secretion of angiogenic and antiapoptotic factors by human adipose stromal cells," *Circulation*, vol. 109, issue 10, pp. 1292-8, 2004.
[36] Hayashi Y, Tsuji S, Tsujii M, Nishida T, Ishii S, Iijima H, Nakamura T, Eguchi H, Miyoshi E, Hayashi N, Kawano S. "Topical transplantation of mesenchymal stem cells accelerates gastric ulcer healing in rats," *American Journal of Physiology-Gastrointestinal and Liver Physiology*, vol. 294, issue 3, pp. 778-86, 2008.
[37] Rashed L, Fayez S. "Therapeutic potential of mesenchymal stem cells in the treatment of gastric ulcer," *Adv. Environ. Biol*, vol. 9, issue 18, pp. 1-7, 2015.
[38] Gong Y, Song L, Yang C, Che Y, Chen Q, Wu B. "The roles of mesenchymal stem cells in gastric lesion and regeneration: applications in gastric diseases," *Acta Gastroenterol. Belg*, vol. 76, pp. 10-4, 2013.
[39] Saleh M, Sohrabpour AA, Mehrabi MR, Seyhoun I, Vaezi AA. "Therapeutic approach of adipose-derived mesenchymal stem cells in refractory peptic ulcer," *Stem Cell Research & Therapy*, vol. 12, pp. 1-9, 2021.
[40] Hassan SA, Abou Elghait AT, Abdelqader ZS, Meligy FY. "Therapeutic efficiency of adipose-derived mesenchymal stem cells in healing of experimentally induced gastric ulcers in rats," *Anatomy & Cell Biology*, vol. 54, issue 3, pp. 361, 2021.
[41] Sayed AH, Mahmoud NS, Mohawed OA, Ahmed HH. "Combined effect of pantoprazole and mesenchymal stem cells on experimentally induced gastric ulcer: implication of oxidative stress, inflammation and apoptosis pathways," *Inflammopharmacology*, vol. 23, pp. 1-22, 2024.
[42] Xia X, Chan KF, Wong GT, Wang P, Liu L, Yeung BP, Ng EK, Lau JY, Chiu PW. "Mesenchymal stem cells promote healing of nonsteroidal anti-inflammatory drug-related peptic ulcer through paracrine actions in pigs". *Science translational medicine*, vol. 11, issue 516, pp. 7455, 2019.
[43] Liu L, Chiu PW, Lam PK, Poon CC, Lam CC, Ng EK, Lai PB. "Effect of local injection of mesenchymal stem cells on healing of sutured gastric perforation in an experimental model," *Journal of British Surgery*, vol. 102, issue 2, pg. e158-68, 2015.
[44] Abd-Elmenm S, Greish S, Atwa M, Fathelbab M. "Evaluation of the role of adiposederived stem cells in the healing of Indomethacininduced gastric ulceration in rats," *J Cell Sci Ther*, vol. 7, issue 4, pp. 1–5, 2016.
[45] El Kasaby A, Ghaly M, Abo Zeid A, Fayed I. "Therapeutic potential of adipose derived mesenchymal stem cells in regeneration of gastric ulcer in rats,". *J Med Histol*, vol. 1, issue 2, pp. 190–201, 2017.
[46] Holm JS, Toyserkani NM, Sorensen JA. "Adipose-derived stem cells for treatment of chronic ulcers: current status," *Stem cell research & therapy*, vol. 9, pp. 1-1, 2018.
[47] Trébol J, Georgiev-Hristov T, Pascual-Miguelañez I, Guadalajara H, García-Arranz M, García-Olmo D. "Stem cell therapy applied for digestive anastomosis: Current state and future perspectives," *World Journal of Stem Cells*, vol. 14, issue 1, pp. 117, 2022.