A COMPARATIVE STUDY ON WOUND HEALING USING PLACENTREX, COLLAGEN, VITAMIN C AND INSULIN

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ABSTRACT

BACKGROUND

The present study was undertaken in Department of Surgery, Jawahar Lal Nehru Medical College and Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha. This study consists of 200 patients of various types of wounds. Equal number of patients of various type of wounds were randomly selected for the local treatment with Placentrex, collagen, vitamin C and insulin. Cleaning and debridement was done to all patients with infected wounds and systemic antibiotic was given according to sensitivity. Results were compared in terms of age, sex incidence, growth of culture organism, formation of healthy granulation tissue, percentage of reduction in size of wound, wound healing and duration of treatment in days/weeks.

MATERIALS AND METHODS

A total of 200 cases of different types of wounds were studied. Patients were divided into four groups containing 50 patients each. A comparative study was done between all the four groups with topical application of Placentrex, Collagen, Vitamin C and Insulin.

RESULTS

It was observed that Mean percentage reduction for Placentrex group was 88.22 ± 8.90 , for Collagen group it was 83.60 ± 12.57 , Insulin group was 37.40 ± 16.26 and for Vitamin C it was 31.80 ± 18.26 . By using one-way ANOVA significant variation is found in all four treatment groups ($F = 212.18$, $p\text{-value} = 0.000$). After comparing all four groups by using TUKEY multiple comparison test significant difference is found between Insulin-Collagen, Insulin-Placentrex, Collagen-Vitamin C and Placentrex-Vitamin C. Mean percentage reduction is more in Placentrex group, hence we can conclude that Placentrex is the best modality of treatment for wound healing.

CONCLUSION

As per this present study in comparison Placentrex is superior in wound healing, collagen is the next best local applicant, vitamin C has some wound healing effects and lastly insulin has negligible results in wound healing.

KEYWORDS

PLACENTREX, Collagen, Vitamin C, Insulin.

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BACKGROUND

The earliest accounts to wound healing dates back to 2000 B.C. when Sumerians first described two methods of wound healing: spiritual and physical, later Joseph Lister made significant contribution by introduction of antiseptics. In some lower animals such as stone crab can regenerate organs with the exception of bone and liver.¹ The body's response to injury leads to release of various chemicals, so called mediators of healing which helps in wound healing. The lost tissue is not regenerated but is replaced by fibrous tissue, the similar events takes place in all the healing process irrespective of the inciting injury. Knowledge of wound healing and various promoters of wound healing allow the

physician to manipulate the wound to achieve an optimal result in a rapid period of time.^{2,3,4}

Wound healing is also dependent on any associated diseases to a major extent and has always been the primary objective of medical care. Many treatments have been used to heal wounds over the years for faster healing and reduced risk of infection. Continuous research has been done and is still undergoing to make safer and efficacious promoters of wound healing.⁵ This study was undertaken with a view to promote healthy granulation tissue, faster and safer wound healing with local application of-

- Placentrex.
- Collagen.
- Vitamin C.
- Insulin.

MATERIALS AND METHODS

The present study was conducted in patients of different kinds of wounds admitted in the surgery ward and also on outpatient basis at AVBR Hospital, Sawangi (Meghe), Wardha after the approval from Ethical Committee of the above Institute. A total of 200 cases of different types of wounds were studied.

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Patients were divided into four groups containing 50 patients each. A comparative study was done between all the four groups with topical application of-

- Placentrex,
- Collagen,
- Vitamin C,
- Insulin.

Patient Selection

All 200 patients were having different types of wounds and on various sites. Care was taken to reduce the various factors which delays wound healing such as diabetic state, haemoglobin levels and peripheral vascular disease.⁶

Patient Preparation

Local hygiene was maintained by cleaning the wound. Systemic antibiotics were administered to all the patients as per culture and sensitivity. All infected wounds were debrided before the local application of these agents. Daily dressing was done and size of the wound including the antero-posterior diameter, transverse diameter and the depth were studied at 7 days, 15 days and 25 days respectively.⁷ Adequate care was taken to keep the factors that delay wound healing to minimal like keeping the sugar levels under control in case of diabetic patients and giving pharmacotherapy in patients of peripheral vascular disease like trental and also improving the haemoglobin levels in case of anaemic patients.^{8,9}

Various Topical Agents used in the Study are as follows- Placentrex

Placentrex is the extract of human placenta. It is available in three forms- 1. Injections, 2. Lotion, 3. Gel form local application of Placentrex gel is used in this study.

Composition

Each gram of Placentrex gel contains extract of human placenta and total nitrogen not more than 0.25% w/w. Placentrex gel is natural vitamins, peptides, nucleotides and amino acid gel.

Pharmacological Properties and Mechanisms of Action of Placental Extract (PLACENTREX)

Wound Healing

Placentrex enhances wound healing significantly; increases collagen synthesis and improves tensile strength of healing tissue. Placentrex brings about maximum increases in the percent of DNA, total protein and epithelialisation.

Anti-Inflammatory

Anti-inflammatory effect involving chemical mediators of the immunological response and analgesic effect have been reported. A CRF-like activity present in extract inhibits phospholipase A2 activity inhibiting formation of arachidonic acid, prostaglandins and leucotrienes.

Collagen

It is major fibrous protein of extracellular connective tissues, and it is also the most ubiquitous and plentiful protein in the animal kingdom. Some 25% - 35% of body protein is collagen. There are 13 types of collagen identified and they are characterised by specific amino acid sequences. The most

abundant and well characterised collagen are Type 1 and Type 3.

Availability of Collagen

Local Application of Collagen for wound healing is available in this study. Collagen is available in sheet form produced from Bovine sources. It is composed mostly of Type 1 and Type 3 collagen.

Salient Features

1. Single application dressing in non-infected cases and clean wounds.
2. Quick and firm adherence.
3. Immediate pain relief.

Mechanism of Action

1. Collagen increases collagen synthesis capacity in granulation tissue of wound.
2. It activates angiogenesis, fibrogenesis, epithelialisation and histomacrophage function.
3. It increases chemoattraction, cell replication and collagen deposition stimulates cell growth, wound healing and tissue augmentation.¹⁰

Vitamin C [Ascorbic Acid]

Chemistry and Source

Ascorbic acid is a 6-carbon organic acid with structural similarity to glucose. It is a potent reducing agent and is biologically active. Citrus fruits (lemon, orange), black currents are richest sources; others are tomatoes, potato, green chillies, cabbage and other vegetables. Human milk is richer in vitamin C (25 – 50 mg/L) than cow's milk.

Physiological Role and Actions

Vitamin C plays a role in many oxidative and other metabolic reactions, e.g. hydroxylation of proline and lysine residues of procollagen- essential for formation and stabilisation of triple helix, formation of intercellular matrix and hydroxylation of carnitine conversion of folic acid to folinic acid.

Therapeutic Uses

1. Prevention of ascorbic acid deficiency in individuals at risk and scurvy,
2. Vitamin C enhances wound healing and can be used to accelerate healing of bed sores, chronic leg ulcer, non-healing ulcer, burns, and postoperatively
3. Anaemia as it enhances the iron absorption.¹⁰

Insulin

Insulin is the hormone secreted by the beta cells of the Islets of Langerhans.

Chemistry

Insulin is a polypeptide with a molecular weight of about 6000 consisting of two amino acid chains A and B, linked by two disulphide bridge. The chains contain 21 and 30 amino acids respectively, all in a known sequence. The disulfide bridges are essential for its biological activity.

Physiological and Pharmacological Actions

1. It stimulates carrier mediated transport of glucose by recruiting glucose transporters (GLUT) from the cytoplasm to the cell membrane.

2. Insulin binds to the specific insulin receptors in the cell membrane of the insulin sensitive and in sensitive cells and activates tyrosine kinase activity, which is inherent in the intracellular part of the insulin receptors.¹⁰

RESULTS

The present study consists of 200 patients of various types of wounds admitted for its management at Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha during the period of April 2006 to September 2008. The observations of the study were as follows.

Sl. No.	Type of Wound	No. of Patients	Percentage
1	Traumatic Wound	82	41%
2	Diabetic Wound	38	19%
3	Peripheral vascular disease related wound	12	6.0%
4	Abscess	12	6.0%
5	Fournier's gangrene	06	3.0%
6	Bed sores	14	7.0%
7	Leprosy	10	5.0%
8	Wound gape	20	10.0%
9	Cellulitis	06	3.0%
Total	200	100%	

Table 1. Shows various Types of Wounds and Number of Patients

From Table No. 1 it is observed that various types of wounds like traumatic, diabetic, peripheral vascular disease, abscess and cellulitis, Fournier's gangrene, bed sore, leprosy, wound gape and other wounds were included in the study and number of patients were 82, 38, 12, 12, 06, 14, 10, 20 and 06 respectively. Among all these, traumatic wounds are found to be common.

Age (Years)	Number of Patients	Percentage
0 - 10	01	0.5%
11 - 20	04	02%
21 - 30	17	8.5%
31 - 40	28	14%

Organisms	Number of Patients									Total	%
	Traumatic	Diabetic	Peripheral Vascular Disease	Abscess	Fournier's Gangrene	Bed Sore	Leprosy	Wound	Cellulitis		
Staph a.	24	11	-	4	-	2	4	4	1	50	25.0%
Pseudomonas sp.	09	2	1				1			13	6.5%
Klebsiella sp.	7	5	-	1	-	-	-	-	-	13	6.5%
E. coli	5	-	-	1	-	4	-	-	1	11	5.5%
E. coli + Staph aureus	3	-	-	-	1		2	2	-	8	4.0%
Pseudomonas+Klebsiella sp.	3	-	-	2	-	-	-	6	-	11	5.5%
Pseudomonas+Staph. a	6	12	-	1	-	1	-	-	-	20	10.0%
Staph.a+Klebsiella.sp.	3	3	-	-	1	2	1	3	1	14	7.0%
Mixed	8	4	6	1	2	1	1	2	1	24	12.0%
Enterobacteria		1	2	-	1	-	-	-	-	4	2.0%
Sterile	14	-	3	2	1	4	1	5	2	32	16.0%
Total	82	38	12	12	6	14	10	20	6	200	100%

Table 4. Showing Distribution of Infecting Organisms found in various Types of Wounds

It has been observed from the above Table 4 that mixed infection was common in all various types of wound. Staphylococci and Klebsiella + Staphylococci were next common organisms cultured from various types of wounds. Other organisms isolated from the wounds were pseudomonas, Klebsiella, proteus and E. coli.

41 - 50	42	21%
51 - 60	54	27%
Above 60	54	27%
Total	200	100%

Table 2. Age and Number of Patients

In the present study, patients of any age were included and grouped at 10 years interval. About 75% patients were above 40 years.

Type of Wound	No. of Male Patients	No. of Female Patients	Total
Traumatic	43	39	82
Diabetic	24	14	38
Peripheral vascular disease	11	1	12
Abscess	8	4	12
Fournier's gangrene	6	-	6
Bed sore	9	5	14
Leprosy	7	3	10
Wound gape	13	7	20
Cellulites	4	2	6
Total	125	75	200
Percentage	62.5%	37.5%	100%

Table 3. Showing various Types of Wounds and Number of Patients according to Sex

Table 3 shows that 125 (62.5%) male patients and 75 (37.5%) female patients were included in the study. Traumatic, abscess and cellulitis related wounds and wound gapes are found to be common in both sexes. Diabetic, peripheral vascular disease is found to be common in male patients. Among the wound related to peripheral vascular disease TAO (Thromboangiitis Obliterans) was a common one. One female patient was presented with peripheral vascular disease due to partial blockage in the right anterior and posterior tibial artery.

Type of Wound	Placentrex	Collagen	Vitamin C	Insulin
Traumatic	28	26	15	13
Diabetic	8	7	13	10
Peripheral Vascular Disease	4	3	3	2
Abscess	2	4	4	2
Fournier's gangrene-	2	2	1	1
Bed sore	2	2	6	4
Leprosy	2	2	2	4
Wound gape	2	2	4	12
Cellulitis		2	2	2
Total	50	50	50	50

Table 5. Showing Method of Local Application and Number of Patients in various Types of Wounds

From the above Table 5, it has been observed that various types of wounds were randomly selected for local treatment with Placentrex, collagen, insulin and vitamin C. Majority of the patients has approximate wound size within 100 sq.cm. Few patients were having approximate wound size within 100 – 120 sq.cm. All these patients were randomly selected for the local treatment with Placentrex, collagen, vitamin C and insulin.

Percentages of Reduction in Size of Wounds	Placentrex	Collagen	Vitamin C	Insulin
No response	-	-	40%	56%
10 - 20%	-	-	24.0%	22%
21 - 30%	-	-	12%	18%
31 - 40%	-	4.0%	12%	4.0%
41 - 50%	-	2.0%	12%	-
51 - 60%	-	2.0%	-	-
61 - 70%	16%	-	-	-
71 - 80%	14%	32%	-	-
81 - 90%	20%	28%	-	-
91 - 100%	50%	32%	-	-

Table 6. Showing Percentage of Reduction in Size of Wounds and comparison of Percentage of Number of Patients treated with Local Application of Placentrex, Collagen, Vitamin C and Insulin

Comparison of Percentage Reduction in Size of Wounds with Local Application of PLACENTREX, Insulin, Collagen and Vitamin C

A. Descriptive Statistics

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
Insulin	50	37.40	16.26	2.30	32.77	42.02	0.00	60.00
Collagen	50	83.60	12.57	1.77	80.02	87.17	60.00	100.00
Placentrex	50	88.22	8.90	1.25	85.68	90.75	60.00	100.00
Vitamin C	50	31.80	18.26	2.58	26.61	36.98	0.00	60.00
Total	200	60.25	29.56	2.09	56.13	64.37	0.00	100.00

From the above Table 6, it is observed that 50% and 32% of patients treated with Placentrex and collagen respectively showed 90% - 100% of reduction in size of wound, whereas 56% and 40% of patients showed no response with the treatment of insulin and vitamin C respectively. Other 50% of patients showed 60% - 90% reduction in size of wound treated with Placentrex, whereas 60% and 8% of patients showed 70% - 90% and 30% - 60% of reduction in size of wound respectively in collagen treated group; 60% of patients treated with vitamin C showed 10% - 50% reduction in size of wound and 44% of patients treated with insulin showed 10% - 40% of reduction in size of wounds.

Total Duration of Complete Treatment (Weeks)	Placentrex	Collagen	Vitamin C	Insulin
0 - 1	4		4	
1 - 2	9	6		
2 - 3	17	6		
3 - 4	6	18	8	
4 - 5	8	10	12	8
5 - 6	6	6	10	22
6 - 7			9	6
Above 7	-	4	7	14
Total	50	50	50	50

Table 7. Showing Duration of Complete Treatment and Number of Patients Treated with Local Application of Placentrex, Collagen, Vitamin C and Insulin

In Placentrex treated group, majority of patients 36 (72%) were treated completely within 1 month and 14 (28%) of patients required 4 - 6 weeks to get complete result. In collagen treated group, 60% of patients were treated completely with 1 month, 32% of patients showed complete treatment within 4 - 6 weeks and 8.0% of patients required more than 7 weeks.

In vitamin C treated group, 36 (72%) patients required 3 - 7 weeks and 7 (14%) patients required more than 7 weeks to show complete treatment. In insulin treated group 36 (72%) patients were completely treated within 4 - 7 weeks and 14 (28%) patients required more than 7 weeks.

B. One-Way ANOVA

Source of Variation	Sum of Squares	Df	Mean Square	F	P-value
Between Groups	132953.41	3	44317.80	212.1	0.000
Within Groups	40936.58	196	208.86	8	HS, p < 0.0001
Total	173889.99	199			

HS- Highly Significant, p < 0.0001

C. Multiple Comparisons: Tukey HSD

Group		Mean Difference (I - J)	Std. Error	P-value	95% Confidence Interval	
					Lower Bound	Upper Bound
Insulin	Collagen	-46.20	2.89	0.000, HS, p < 0.0001	-53.68	-38.71
	Placentrex	-50.82	2.89	0.000, HS, p < 0.0001	-58.30	-43.33
	Vitamin C	5.60	2.89	0.216, NS, p > 0.05	-1.88	13.08
Collagen	Placentrex	-4.62	2.89	0.382, NS, p > 0.05	-12.10	2.86
	Vitamin C	51.80	2.89	0.000, HS, p < 0.0001	44.31	59.28
Placentrex	Vitamin C	56.42	2.89	0.000, HS, p < 0.0001	48.93	63.90

From the above table, it was observed that mean percentage reduction for Placentrex group was 88.22 ± 8.90 , for Collagen group it was 83.60 ± 12.57 , Insulin group it was 37.40 ± 16.26 and for Vitamin C it was 31.80 ± 18.26 . By using One-Way ANOVA significant variation is found in all four treatment groups (F= 212.18, p-value= 0.000).

DISCUSSION

In Placentrex treated group, 80% of patient's wound treated with Placentrex healed completely and does not require any secondary operative procedure. In 20% of patients, due to larger size wound skin grafting was required.¹¹

In collagen treated group, 50% of patients' wound healed completely and 28% of patients required skin grafting and 22% of patients required resuturing.

In vitamin C and insulin treated group majority of patients showed no response or minimal reduction in size of wound, so all patients were treated with vitamin C and insulin were required for skin grafting or resuturing according to wound size.

In Placentrex treated group, majority of patients were completely treated within one month and only few patients required 4 - 6 weeks to show complete treatment. In collagen treated group, majority of patients showed complete response within one and a half month and only one patient required more than 7 weeks to show complete response.

Duration of complete treatment was increased in insulin and vitamin C treated group as compared to Placentrex and collagen treated patients.

In Patients treated with Placentrex following Advantages were noted-

1. It promotes early healthy granulation tissue, epithelialisation and healing.
2. It combats infections and reduces the incidence of infection.
3. Relief from pain.
4. It is nontoxic and non-antigenic.
5. It is economical.
6. It has simple method of application.

Collagen is the next best local applicant; it also promotes healthy granulation tissue; 50% of patients showed complete wound healing and reduces hospital stay.^{12,13}

Next to collagen vitamin C has some wound healing effect, as majority of patients showed 10% - 50% reduction in size of wound one month after the treatment with vitamin C. Insulin has minimal wound healing effects as 50% of patients showed no response and other 50% of patients showed very minimal reduction in size of wound. In both vitamin C and insulin treated group, patients required longer healing duration.¹²

Mean percentage reduction for Placentrex group was 88.22 ± 8.90 , for Collagen group it was 83.60 ± 12.57 , Insulin group was 37.40 ± 16.26 and for Vitamin C it was 31.80 ± 18.26 . By using one-way ANOVA significant variation is found in all four treatment groups (F = 212.18, p-value = 0.000).

After comparing all four groups by using TUKEY, multiple comparison test significant difference is found between Insulin-Collagen, Insulin-Placentrex, Collagen-Vitamin C and Placentrex-Vitamin C. Mean percentage reduction is more in Placentrex group, hence we can conclude that Placentrex is the best modality of treatment for wound healing.

As per this present study in comparison, Placentrex is superior in wound healing, collagen is the next best local applicant, vitamin C has some wound healing effects and lastly insulin has negligible results in wound healing.

CONCLUSION

After comparing all four groups by using TUKEY multiple comparison Test, significant difference is found between Insulin-Collagen, Insulin-Placentrex, Collagen-Vitamin C and Placentrex-Vitamin C. Mean percentage reduction is more in

Placentrex group; hence, we can conclude that Placentrex is the best modality of treatment for wound healing.

As per this present study in comparison, Placentrex is superior in wound healing; collagen is the next best local applicant; vitamin C has some wound healing effects and lastly insulin has negligible results in wound healing.

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