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Evaluation of Biochemical and Cytological Analysis of Drain Fluid after Modified Radical Mastectomy

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ABSTRACT

Background: Axillary lymph node dissection (ALND) has long been an integral part of the management of carcinoma breast. Post operative prolonged axillary drainage and seroma is most common sequelae following ALND. The etiology of prolonged axillary drainage and seroma is yet not clear.

Objective: To study the biochemical and cytological nature of fluid after modified radical mastectomy and change in composition of axillary drain fluid over prolonged drainage period.

Study design: Prospective study.

Material and methods: Fifty patients of carcinoma breast who underwent modified radical mastectomy (MRM) in department of surgery, PGIMS Rohtak were included in the study. Axillary drain fluid was analysed by cytology and biochemistry. The total cell count, differential cell count, proteins, triglycerides and cholesterol levels were evaluated.

Observations: Mean age of patients was 52 years. Mean axillary drain output was 908.9ml (range 240-1830 ml). Mean duration of axillary fluid drainage was 8.94 days. Drainage fluid increases with increase in age and it was statistically significant($p=0.015$). No significant correlation was found between axillary fluid output and duration with BMI, T tumor, lymph node involvement and neoadjuvant chemotherapy. Polymorphs dominated first 5 days but on day 7 the fluid was rich in lymphocytes which increased constantly thereafter. Protein was more than 2.5 in first 5 days and later on it was in decreasing trend. Cholesterol levels were >45mg/dl on day 1 and it reduced to <45mg/dl by day 3.

Conclusion: Both inflammatory and lymphatic fluid were present in axillary drain from the beginning but since inflammatory process dominated the initial few days of post operative period as a part of normal wound healing process. This resulted in masking of lymphatic nature of fluid which became obvious after inflammation settled down.

Key words: Modified radical mastectomy(MRM), drain fluid.

INTRODUCTION

Cancer has become a major source of morbidity and mortality globally.[1] One in eight women born today will be diagnosed with breast cancer at some time in her life.[2] Breast cancer can be treated using a multimodality approach of surgery, chemotherapy, radiotherapy and targeted therapy. The treatment options vary as per the stage of the tumor. Surgical treatment for breast cancer includes breast conservation therapy and mastectomy with or without axillary dissection depending on disease stage. One of the most common sequelae and cause of morbidity following ALND is prolonged post operative axillary drainage and seroma which might even take several weeks to resolve completely.[3] Although seroma is not life threatening, it can lead to significant morbidity (e.g. flap necrosis, wound dehiscence,sepsis, prolonged recovery period, multiple physician visits) and may delay adjuvant therapy. The origin of seroma is unclear.[4] Studies on the

composition of the fluid collected from post mastectomy drainage suggested its inflammatory origin while others hypothesized that seroma is most likely to originate from lymph. The aim of our prospective observational study was to determine the nature of axillary drainage fluid and to study the change in composition of axillary drainage fluid with prolonged drainage, in patients with breast cancer undergoing ALND.

MATERIAL AND METHODS

This prospective study was conducted in fifty female patients of carcinoma breast who underwent modified radical mastectomy (MRM). The patients having prior axillary surgery, prior radiotherapy, concurrent treatment with skin grafting and simultaneous breast reconstruction surgery were excluded from the study. Following parameters were evaluated:

1. Cell counts, total counts, differential cell counts, proteins, triglycerides and cholesterol levels of axillary drain fluid was done on every alternate day till 14 days or till the drain is not removed, whichever was earlier.
2. Culture and sensitivity of axillary fluid on day 5.
3. Axillary drain output, the number of days of drainage and total axillary drainage for each patient was recorded daily.

The flap drain was removed after 48 hrs and axillary drain was removed when drainage amount was less than 20ml/24 hrs. Data was calculated, tabulated and analyzed using ANOVA and t- test to evaluate the biochemical and cytological analysis of drain fluid after modified radical mastectomy.

OBSERVATIONS

All 50 patients included in study were females. The age of patients varied between 28 and 75years with mean age of 52±12.7. Majority of cases were between 41 to 60 years. All patients presented as lump in breast.

Sixteen patients had normal BMI (17.50-22.99), while 34 patients were either overweight or obese according to Asian guidelines of obesity (overweight-23.0-27.99 obese->28.0). In 25 patients (50%) neoadjuvant chemotherapy was given. One patient (2%) had T1 tumor, majority of patients (44%) had T2 tumor, 21 patients (42%) had T3 and 6 patients (12%) had T4 tumor. Clinically, 15 patients (30%) had no palpable lymph node, while majority of patients had (56%)N1 status, 7 patients (14%) had N2 status and none of the patients had N3 status.

Total axillary drain output varied between 240 and 1830 ml with the mean output of 908.9±421.55 ml. Mean duration of axillary fluid drainage was 8.94±1.42 days. Pattern of drain output showed a constant decrease in amount of axillary fluid. Correlation coefficient of BMI with duration of drainage (in days) was (r=0.018) insignificant (0.903). There was an increase in axillary fluid with increase in age. Pearson's correlation coefficient value 'r'=0.341 was significant (p-0.015).

Mean drain output increase with T tumor. But it was not statistically significant (p-0.612). There was no significant difference between the axillary fluid output when compared with biopsy proven node status (p-0.518). We didn't find any correlation in axillary drain output duration and lymph nodes status (p-0.355). There was no significant difference between the axillary fluid output among the patients who received neoadjuvant therapy or not (p-0.208).

RBC were positive in drain fluid of all the 50 patients till post op day 5 and after that RBCs were seen in drain fluid of 43 patients and negative in 7 patients while drain was already removed in 4 patients, on post op day 9 RBC was seen in none of drain fluid. Upto day 3, protein was more than 2.5 and from 5^{th} day onwards it was less than 2.5. Here, ANOVA test was applied and p value for protein in the drain fluid was (<0.001) statistically significant.

Upto day 5, polymorphs dominated (62.89%) and afterwards lymphocytes dominated (51.6%) in drain fluid. ANOVA test was applied and p values of the change in pattern of cell count was calculated $p<0.05$.

Cholesterol level was more than 45 on day1(47.49) which suggest that fluid was inflammatory in origin on day 1 and it was less than 45 on post op day3(41.98) suggesting shift to lymphatic nature on day 3. Constant decrease in TG and HDL level suggest that fluid was initially inflammatory. ANOVA test was applied and p values of change of pattern were calculated and it came out significant for TG, cholesterol and HDL, while it was insignificant for LDL.

DISCUSSION

The age of presentation of the patients in our study group was between 28 and 75years and its pearson's correlation coefficient value was 'r'=0.341 with drain output which was significant (p-0.015). However, this correlation of drain output with age was weak. This finding was consistent with the study conducted by Kumar et al who concluded age as very important risk factors associated with prolonged drainage.[5] However, a study conducted by Kuroi et al advocated no relationship between age of the patient and axillary drain output.[6]

There was no significant difference between the axillary fluid output and duration of days when compared on the basis of node status (p-0.518). Comparison between the Correlation coefficient of Lymph node status with drain output (r = -.093) was insignificant. This finding was consistent with the finding of Hashmi et al who showed no association of lymph node involvement and amount of axillary fluid.[4] But Petrek et al showed axillary lymph node involvement as most significant risk factor.[7]

We found no significant difference between the axillary fluid output when compared on the basis of chemotherapy given or not (p-0.208). Comparison between the Correlation coefficient of Lymph node status with drain output was r = -.051 which was insignificant (p-0.725). This finding was consistent with Woodworth et al, Petrek et al and Gonzalez et al who found no association of neoadjuvant therapy and axillary drain fluid amount.[7,8,9]

On analyzing the biochemical and cytological parameters of the axillary fluid, it was found that the predominant cells in the axillary fluid were polymorphs (2256.6 on day 1) up to day 5 suggesting that axillary drain fluid is an exudate not lymph. Also high value of protein (3.43 on day1) initially supports that axillary fluid is inflammatory origin. Also the value of cholesterol (47.49 0n day1) suggests that it is inflammatory initially that occurs during the initial phase of wound repair. However on day 7, the lymphocytes dominated the axillary cytology with constant reduction in total protein. This suggests that overriding inflammation related to surgical trauma abates by 7th day and only lymphatic fluid drainage remains to be drained.

Table 1: Comparison of Different Studies Related to Seroma

STUDY DONE	SAMPLE SIZE	PARAMETERS USED
Bonnema et al[10]	16	Electrolytes, Total protein, albumin, Globulin, Hemoglobin, Transferrin, igG, Fibrinogen, lipids, Blood cells, Glucose, Osmolality, Creatinine and phoshokinase
Tadyeh et al[11]	2	Protein and Cell count
Watt Boolsen et al[12]	27	Number of leucocytes, granulocytes, lymphocytes, and IgG
McCaul et al[13]	18	Blood cells, Total protein, Albumin, Globulin, lipids, Calcium, Gamma glutamyl transferase and Aspartate amino transferase
Wu et al[14]	16	VEGF and Endostatin
Jain et al[15]	37	Protein and LDH
Present Study	50	Cell count, total proteins and lipids

Various studies suggest that there is no consensus about the nature and etiopathogenesis of axillary drainage fluid and of any change in its composition with prolonged drainage. There is an incomplete knowledge of factors that influence prolonged axillary drainage If the fluid is lymphatic nature, it is important to prevent lymph leakage during and after mastectomy, whereas if it is inflammatory, care should be taken to minimize the intensity and duration of the first phase of repair. Although seroma is not life threatening, it leads to significant morbidity in the form of flap necrosis, wound dehiscence, sepsis, prolonged recovery period, multiple clinician visits and may delay adjuvant therapy.[16] Knowledge of nature of axillary fluid can be an aid in planning preventive strategies against seroma formation.

CONCLUSION

Both inflammatory and lymphatic fluid were present in axillary drain from the beginning but since inflammatory process dominated the initial few days of post operative period as a part of normal wound healing process. This resulted in masking of lymphatic nature of fluid which became obvious after inflammation settled down. While amount of drain output was directly correlated with age, BMI, T stage, N stage and neoadjuvant chemotherapy, statistically significant association was found only with age. Small sample size of present study is a limitation. Future research on axillary drain fluid after MRM is needed to make things more clear.

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